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RELATIONSHIP OF TONSILS AND ADENOIDS TO THE TYPE OF POLIOMYELITIS

AN ANALYSIS OF FOUR HUNDRED AND THIRTY-TWO CASES

PASCAL F. LUCCHESI, M.D., M.P.H., AND ALFRED C. LABOCETTA, M.D.

PHILADELPHIA

Since Ayer,¹ in 1928, and Aycock and Luther,² in 1929, reported instances of poliomyelitis following recent tonsillectomy, there have been a number of papers on this subject. Many of the observers were able to show that the removal of tonsils and adenoids during a season in which poliomyelitis was prevalent made the patient more susceptible to the disease, and they considered the operative wound as a portal of entry for the virus.

No. of Cases

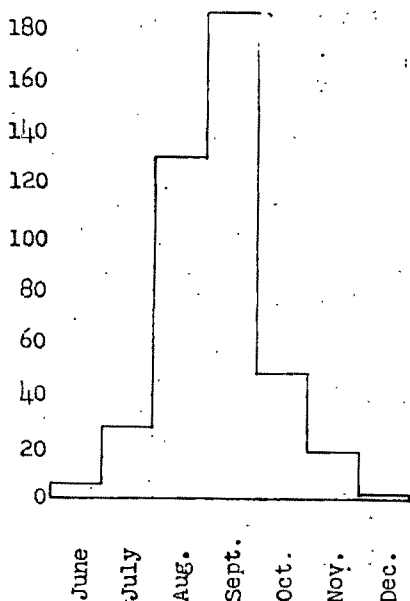


Fig. 1.—Monthly distribution of time of onset of poliomyelitis for 432 cases occurring from 1937 to 1942 inclusive.

Fischer, Stillerman and Marks³ and Top and Vaughan⁴ have since studied the status of tonsils

From the Philadelphia Hospital for Contagious Diseases.

1. Ayer, W. D.: Poliomyelitis Proc. Internat. Assemb. Inter-State Post-Grad. M. A. North America 29:319, 1928.

2. Aycock, W. L., and Luther, E. H.: The Occurrence of Poliomyelitis Following Tonsillectomy, New England J. Med. 200:164 (Jan. 24) 1929.

3. Fischer, A. E.; Stillerman, M., and Marks, H. H.: Relation of Tonsillectomy and of Adenoidectomy to the

and adenoids relative to the incidence of acute poliomyelitis and have observed that tonsils and adenoids were frequently absent in patients with involvement of the higher centers. The purpose of the present study is to determine the relationship that the presence or absence of tonsils bears to the type of disease acquired and to mortality.

MATERIAL

The material for this study included 432 patients admitted to the Philadelphia Hospital for

No. of Cases

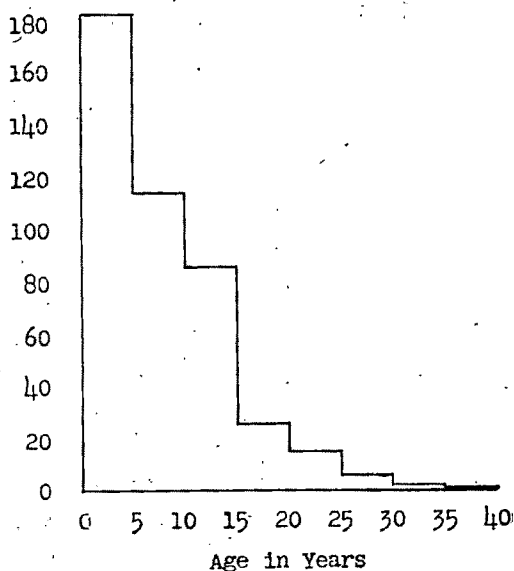


Fig. 2.—Distribution of 432 cases of poliomyelitis according to the ages of the patients.

Contagious Diseases with acute anterior poliomyelitis from 1937 to 1942 inclusive. The number of patients admitted yearly ranged from 9 to 177, and the monthly distribution was the same each year, that is, admissions during August and September predominated (fig. 1).

Incidence of Poliomyelitis, with Special Reference to the Bulbar Form, Am. J. Dis. Child. 61:305 (Feb.) 1941.

4. Top, F. H., and Vaughan, H. F.: Epidemiology of Poliomyelitis in Detroit in 1939, Am. J. Pub. Health 31:777 (Aug.) 1941.

TABLE 1.—Seasonal Distribution of the Types of Poliomyelitis Based on the Records of Four Hundred and Twenty-Seven Patients (1937 to 1942 Inclusive)

Type of Poliomyelitis	Adenotonsillar Status of Patient	June	July	Aug.	Sept.	Oct	Nov.	Dec.	Total
Spinal	T&A *	3	1	36	40	13	5	..	98
	None	3	22	62	88	33	9	2	219
Bulbar	T&A	8	11	3	1	..	23
	None	2	3	2	7
Bulbospinal	T&A	..	1	6	13	6	..	1	28
	None	..	3	5	7	1	2	..	18
Nonparalytic	T&A	6	8	..	1	..	15
	None	5	14	0	19

* T&A indicates patients who had had adenoidotonsillectomy. None indicates patients who had not had adenoidotonsillectomy.

TABLE 2.—Types of Poliomyelitis Occurring in Nineteen Tonsillectomized Patients Under Six Years of Age

Age of Patient, Yr.	Interval *	Type of Poliomyelitis
2	1 year	Bulbar
4	Unknown	Spinal
4	1 year	Spinal
4	3 weeks	Bulbospinal
4	6 months	Spinal
4	3 months	Bulbar
5	2 years	Bulbospinal
5	Same year	Bulbar
5	6 months	Bulbar
5	2 years	Nonparalytic
5	1½ years	Bulbar
5	2 years	Spinal
5	1 year	Spinal
5	4 months	Spinal
5	1 month	Spinal
5	1 year	Spinal
5	1 year	Bulbospinal
5	7 months	Spinal
5	1 year	Spinal

* Between adenoidotonsillectomy and onset of first symptom of poliomyelitis.

TABLE 3.—Data for Patients Who Died of Poliomyelitis from 1937 to 1942 Inclusive

Age of Patient, Yr.	Sex of Patient	Race of Patient	Adenoidotonsillectomy	Date of Onset of Illness	Interval Between Adenoidotonsillectomy and Onset	Date of Death	Type of Poliomyelitis
11	M	White	Yes	9/ 5/37	Unknown	9/30/37	Bulbospinal
10	M	Negro	No	9/ 5/37	—	9/2/37	Bulbospinal
11	M	White	1931	10/ 4/37	6 years	10/ 5/37	Bulbospinal
21	F	White	Yes	9/ 5/38	Unknown	9/2/38	Spinal
7	F	White	1933	9/10/38	Unknown	9/2/38	Bulbospinal
12	M	White	1931	10/12/38	7 years	10/2/38	Bulbospinal
14	M	White	1932	7/15/38	7 years	7/30/39	Bulbospinal
14	M	White	1930	8/ 4/39	9 years	8/2/39	Bulbar
11	M	White	1935	8/30/39	4 years	9/ 7/39	Bulbospinal
16	F	White	No	9/ 9/39	—	9/3/39	Bulbospinal
10	F	White	1936	10/18/39	3 years	10/21/39	Bulbospinal
14	M	White	No	10/11/39	—	10/16/39	Spinal
10	F	White	1933	9/ 7/40	2 years	9/11/40	Bulbar
2	M	White	No	9/ 3/40	—	9/ 6/40	Spinal
12	M	White	1935	9/25/40	4 years	9/30/40	Bulbar
11	M	White	1931	9/24/40	9 years	10/29/40	Spinal
24	M	White	1923	9/27/40	12 years	11/30/40	Spinal
30	F	White	1921	12/31/40	Unknown	1/ 5/41	Bulbospinal

THE TYPES OF POLIOMYELITIS AND THEIR RELATIONS TO VARIOUS FACTORS

The term "spinal poliomyelitis" is used to designate the condition in which only the spinal cord is involved. The term "bulbar poliomyelitis" is used for the condition in which cranial nerves only are involved. The condition in which both the cranial nerves and the spinal

cord are involved is classified as "bulbospinal poliomyelitis." Poliomyelitis without weakness or paralysis is referred to as "nonparalytic."

Season.—The type of poliomyelitis that occurred was related to the season; that is, spinal poliomyelitis, which is the most common type, was the first to appear (July and August) and the last to disappear (November and December), whereas bulbar, bulbospinal and nonparalytic poliomyelitis more frequently appeared in August and September, when the season was at its height.

Race.—Of the total number of patients 10.9 per cent were Negroes and 89.1 per cent were white. The percentage of Negroes in the total population under 15 years of age according to the 1940 census for Philadelphia was 15.6. Five of the 48 patients with bulbospinal poliomyelitis and 8 of the 35 with nonparalytic poliomyelitis were Negroes. There were no Negroes with the bulbar type.

Twelve (26.1 per cent) of the Negro patients had no tonsils and adenoids. Of this group 2 had nonparalytic poliomyelitis and 10 had the spinal type.

Sex.—About two thirds of the patients were males, a proportion which was constant for the different types of poliomyelitis. The mortality was the same for patients of the two sexes. Forty and five-tenths per cent of all the male and 35.4 per cent of all the female patients had had their tonsils and adenoids removed at some time in the past.

Age of the Patient.—Patients under 6 years constituted the largest age group. The incidence of the disease had an inverse relationship to age. The youngest patient was 8 months old, and the oldest was 38 (fig. 2).

Tonsillectomy and Adenoidectomy.—Data on tonsillectomies and adenoidectomies were not obtained in 5 of the 432 cases. There were 19

patients under 6 years of age who had had their tonsils and adenoids removed, and 8 of these children (41 per cent) had bulbar involvement. On the other hand, of 161 patients in the non-adenoidotonsillectomized group under 6 years of age, only 13 (8.1 per cent) had bulbar involvement.

Mortality.—Eighteen of 432 patients died. Of these 3 had bulbar, 5 had spinal and 10 had bulbospinal poliomyelitis. Fourteen of the patients who died (78 per cent) had had tonsillectomy and adenoidectomy.

TABLE 4.—*Mortality According to the Type of Poliomyelitis*

Type	Number of Cases	Number of Deaths	Number of Deaths per Hundred Cases
Spinal.....	319	5	1.3
Bulbar.....	30	3	10.0
Bulbospinal.....	48	10	20.3
Nonparalytic.....	35	0	0.0
Total.....	432	18	4.2

TABLE 5.—*Incidence of Poliomyelitis of Each of the Four Types According to the Presence or Absence of Tonsils and Adenoids*

Type	Total Number of Patients	Patients Without Tonsillectomy		Patients With Tonsillectomy	
		No.	%	No.	%
Spinal.....	317	219	69.1	98	30.9
Bulbar.....	30	7	23.3	23	76.7
Bulbospinal.....	48	13	27.1	35	72.9
Nonparalytic.....	34	19	55.9	15	44.1
Total.....	427	263	61.6	164	38.4

Over 76 per cent of the patients with bulbar poliomyelitis and 61 per cent of those with bulbospinal poliomyelitis had had an adenoidotonsillectomy, while only 30.9 of the patients with only spinal involvement had had their tonsils and adenoids removed. Nonparalytic poliomyelitis occurred in about equal proportions of the adenoidotonsillectomized and the nonadenoidotonsillectomized patients.

There is a greater tendency toward involvement of the higher centers in poliomyelitis in patients without tonsils and adenoids. Table 6 shows that the higher incidence of bulbar and bulbospinal poliomyelitis in patients without tonsils and adenoids occurs in all age groups but is least pronounced in the group over 15 years of age.

In the 0 to 5 years age group only 8.1 per cent of the nontonsillectomized patients had bulbar or bulbospinal poliomyelitis, as against 42 per cent of the tonsillectomized patients; this age group presents the greatest contrast in the incidence of involvement of the higher centers. In the 6 to 10 year age group bulbar involvement occurred in 16 per cent of the nontonsillectomized and in 33.9 per cent of the tonsillectomized patients, and in the 11 to 15 year age group, in 9.7 and 33.2 per cent respectively.

COMMENT

The data reviewed represent the nonepidemic incidence of poliomyelitis in a large city over a period of six years and include material concerning only those patients who were admitted

TABLE 6.—*Incidence of Poliomyelitis of Each of the Four Types in Patients With (165) and Without (252) Adenoidotonsillectomy*

	Number of Cases								Percentage			
	0-5 Years		6-10 Years		11-15 Years		Over 15 Years		0-5 Years	6-10 Years	11-15 Years	Over 15 Years
	M	F	M	F	M	F	M	F				
Patients without adenotonsillectomy												
Spinal.....	91	46	16	21	16	10	9	9	85.1	74.0	83.8	96.0
Bulbar.....	2	2	3	2	2.5	6.0
Bulbospinal.....	6	3	3	1	2	1	..	1	5.6	10.0	9.7	5.0
Nonparalytic.....	7	4	3	5	1	1	..	1	0.8	10.0	6.5	5.0
Total.....	106	55	25	29	19	12	9	11	100	100	100	100
Patients with adenotonsillectomy												
Spinal.....	4	6	20	12	23	8	12	12	52.6	54.8	57.4	80.0
Bulbar.....	4	1	7	1	7	..	1	1	26.3	14.5	13.0	6.7
Bulbospinal.....	2	1	9	5	8	3	..	2	15.8	19.4	20.4	6.7
Nonparalytic.....	1	..	4	..	5	..	2	..	5.3	11.3	9.3	6.7
Total.....	11	8	40	28	43	11	15	15	100	100	100	100

The mortality was lowest for patients with spinal and highest for those with bulbospinal poliomyelitis.

Table 5 shows the incidence of poliomyelitis of each of the four types defined in 164 adenoidotonsillectomized patients and in 263 patients with intact tonsils and adenoids.

to the Philadelphia Hospital for Contagious Diseases. In the same period 544 cases and 38 deaths were reported to the city health department. Admittedly the number of cases studied is small, but the consistency of the data adds weight to the belief that a positive correlation exists between absence of pharyngeal lymphoid

tissue and involvement of the higher centers in poliomyelitis.

There has been much criticism of data on this subject by persons who believe that an adenoid-tonsillectomy must occur within the incubation period of the disease in order to have any effect on the course of the illness. It is interesting to note that the disease developed within one month after the removal of tonsils and adenoids in only 3 of our patients and that of these 2 had bulbar symptoms.

This review reveals that tonsils and adenoids are absent in a significantly high percentage of patients who have bulbar or bulbospinal poliomyelitis. The absence of adenoid-tonsillar tissue apparently increases the likelihood that the bulbar centers will be involved when a susceptible person becomes infected with the virus of poliomyelitis. Hence it may be assumed that Waldeyer's ring inhibits the passage of the virus through the pharyngeal structures. It may be possible that by leaving the tonsils and adenoids in situ the incidence of poliomyelitic infection of the higher centers, which causes the highest mortality, can be reduced. In support of this assumption it will be noted that 78 per cent of the 9 patients in the 11 to 15 year age group who died had bulbar symptoms and had no tonsils or adenoids.

It may be inferred from the evidence in this study that the absence of tonsils and adenoids increases the risk of bulbar and bulbospinal involvement in persons with poliomyelitis. Consequently the indiscriminate removal of tonsils and

adenoids should not be condoned. It would be wise to postpone the removal of tonsils and adenoids during the season and in areas in which the incidence of poliomyelitis is abnormally high, if for no other reason than to have these structures act as a protective barrier.

We realize that the relationship between the absence of tonsils and adenoids and the incidence of involvement of the higher centers may be coincidental, that a cause and effect relationship has not been established and that an unknown factor may be the cause.

SUMMARY AND CONCLUSIONS

Four hundred and thirty-two cases of acute anterior poliomyelitis were reviewed to determine the relationship of the presence or absence of tonsils and adenoids to the type and to the mortality of the disease. The incidence of bulbar and bulbospinal poliomyelitis was significantly higher in patients without than in patients with tonsils and adenoids.

The mortality was 10.9 times greater in the patients with bulbar symptoms than in those with nontulbar poliomyelitis.

It is recommended that tonsils and adenoids be not removed unless the removal is specifically indicated.

Addendum: At the Philadelphia Hospital for Contagious Diseases in 1943 there were 17 cases of poliomyelitis, 1 nonparalytic, 1 bulbar, 3 bulbospinal and 12 spinal. All the patients with bulbar involvement were without tonsils.

400 North Front Street.

Philadelphia Hospital for Contagious Diseases

SULFADIAZINE IN THE TREATMENT OF DIARRHEA IN CHILDREN

FRANCISCO J. MENCHACA, M.D.

SANTA FE, ARGENTINA

Sulfonamide compounds are more widely used every day for the treatment of diarrhea in children, especially in countries in which infection is the most important cause of diarrhea.

The optimal use of the various sulfonamide compounds in treating the different forms of diarrhea has not yet been determined. New therapeutic agents are being produced rapidly, and the pharmacologists continue to search for new compounds of greater efficiency. It devolves on pediatricians to present clinical observations on the use of these compounds as guides to the value of each preparation.¹ It is for this reason that I wish to record my results with sulfadiazine, following earlier reports on sulfathiazole,² sulfaguanidine,³ and succinylsulfathiazole.⁴

Up to the present time there have been few reports on the use of sulfadiazine in the treatment of diarrhea in children. Abente Haedo and Rodríguez Devincenzi⁵ were successful in the treatment of 3 children with bacillary dysentery and 2 with diarrhea due to *Salmonella*. In June 1943 Richard Tudor⁶ published observations on the use of sulfadiazine and sulfapyrazine for infantile diarrhea in which the stools in some cases showed bacillary dysentery. Of the children treated with sulfadiazine, 3 had serious, 4 had moderate and 3 had mild dehydration. The results were satisfactory; the mortality was reduced to zero and the average

number of days required for cure was three and nine-tenths.

There are some experimental reports on the action of sulfadiazine against intestinal microorganisms. (Strauss and Finland⁷ found that sulfathiazole and sulfadiazine were bactericidal against *Escherichia coli*, *Shigella paradysenteriae* (Flexner), *Salmonella cholerae suis*, *Salmonella enteritidis*, *Salmonella Schottmuelleri* and *Salmonella typhi murium*. At a higher concentration they showed bacteriostatic action against *Salmonella paratyphi*. The same authors, in other experiments on the action of the sulfonamide compounds on *E. coli* in a synthetic medium, found that sulfadiazine and sulfathiazole were the most active, while sulfapyridine, sulfaguanidine and sulfanilamide were less effective, in the order named.)

Neter⁸ has produced evidence that sulfadiazine, as well as sulfanilamide, sulfapyridine and sulfaguanidine, is capable of delaying the secondary development of *Shigella dysenteriae* and *E. coli* in broth containing bacteriophages.

White⁹ tested the activity of various sulfonamide drugs against the intestinal coliform flora. He listed them in the following descending order of activity: sulfapyrazine, sulfadiazine, sulfathiazole, N¹-acetylsulfanilamide, sulfaguanidine, sulfanilylarsanilic acid, succinylsulfathiazole and sulfanilamide.

Klinefelter¹⁰ inoculated rats intraperitoneally with a culture of *E. coli*. They were given 1 per cent of sulfathiazole or 0.7 per cent of sulfadiazine in their food. The latter drug proved more efficacious than the former.

7. Strauss, E., and Finland, M.: Bacteriostatic and Bactericidal Action of Sulfadiazine in Vitro on Gram-Negative Bacteria, *Proc. Soc. Exper. Biol. & Med.* **47**: 432, 1941.

8. Neter, E.: Inhibitory Effect of Sulfonamide Compounds upon Development and Growth of Phage-resistant Bacteria, *Proc. Soc. Exper. Biol. & Med.* **47**: 20, 1941.

9. White, H. J.: Comparative Activity of Sulfonamides Against Coliform Bacteria in the Intestine of Mice, *Bull. Johns Hopkins Hosp.* **71**: 213, 1942.

10. Klinefelter, H. F.: Sulfadiazine: Effect on *E. Coli* Infections in Mice, *Proc. Soc. Exper. Biol. & Med.* **46**: 591, 1941.

1. Menchaca, F. J.: Los derivados sulfonamídicos en el tratamiento de las diarreas infantiles, Buenos Aires, El Ateneo, 1943, p. 17.

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3. Menchaca, F. J.: La sulfaguanidina en diarreas infantiles de la ciudad de Santa Fe, *Arch. argent. de pediat.* **16**: 473, 1941.

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5. Abente Haedo, F., and Rodríguez Devincenzi, A.: La sulfadiazina en la shigelosis y en la salmonelosis, *An. Fac. de med. de Montevideo* **27**: 449, 1942.

6. Tudor, R. B.: Chemotherapy of Infantile Diarrhea: Comparison of Sulfadiazine and Sulfapyrazine, *J. Pediat.* **22**: 652, 1943.

In a paper on the activity of sulfathiazole, sulfadiazine, sulfapyrazine and sulfanilamide against *E. coli*, White, Litchfield and Marshall¹¹ reported that sulfapyridine was sixteen times and sulfathiazole and sulfadiazine were sixty-four times more active than sulfanilamide.

PROCEDURE

(I decided to employ sulfadiazine¹² for patients with infantile diarrhea entering the children's service under my charge. Most of them had severe or moderate diarrhea that had not improved under treatment in out-patient clinics.

I tried as far as possible to systematize the therapy. Injections of isotonic solution of sodium chloride with dextrose were given, and isotonic solution of three chlorides with 3 per cent dextrimaltose was administered by mouth. The diet consisted of either buttermilk with dextrimaltose or human milk. Only 2 patients received plasma, and the use of antidiarrheics was avoided.

A total of 0.1 to 0.15 Gm. of sulfadiazine per kilogram of body weight was given daily in four doses, six hours apart. I could not begin the treatment with sodium sulfadiazine by intravenous injection, as is recommended for the initial treatment of severe attacks, because the sodium salt was not available.)

As is seen in the table of clinical data, there were no deaths. The average time required for recovery was five and nine-tenths days. It is self evident that the determination of the

11. White, H. J.; Litchfield, J. T., Jr., and Marshall, E. K., Jr.: Quantitative Comparisons of Activity of Sulfanilamide, Sulfapyridine, Sulfathiazole and Sulfadiazine Against *Escherichia Coli* in Vivo and in Vitro, *J. Pharmacol. & Exper. Therap.* **73**:104, 1941.

12. The sulfadiazine used was furnished by Lederle Laboratories.

time of recovery was somewhat subjective; however the observations were all made by one person. Dysentery bacilli and salmonellas were absent from the stools (examined by Dr. J. Belloc). There was no sign of intolerance to the drug. In some instances the stools became gray.

RESULTS

Table of Clinical Data

Patient	Age, Mo.	Weight, Gm.	Stools in Last 24 Hr.	Dehydration	Time Required to Improve Stools, Days	Outcome
1	3	4,320	6 or 7	Notable	7	Recovery
2	5	7,350	6	Mild	3	Recovery
3	2	3,830	7	Notable	4	Recovery
4	2	3,150	7	Notable	5	Recovery
5	4	5,400	6 or 7	Notable	15	Recovery
6	3	4,520	6	Mild	12	Recovery
7	17	8,000	4	None	4	Recovery
8	8	4,860	10	Notable	14	Recovery
9	6	6,330	7	None	1	Recovery
10	4	3,900	7	Notable	4	Recovery
11	2	3,470	7	Notable	6	Recovery
12	10	6,880	17	Notable	4	Recovery
13	8	7,080	3	Mild	4	Recovery
14	30	13,600	6	Mild	5	Recovery
15	3	4,100	5	Notable	8	Recovery
16	12	6,980	7	Notable	2	Recovery
17	5	3,280	3	Notable	6	Recovery
18	9	5,650	8	None	3	Recovery
19	5	5,930	5	Mild	3	Recovery
20	5	4,610	7 or 8	Notable	9	Recovery

CONCLUSIONS

(From the observation of 20 children with diarrhea treated with sulfadiazine I think that it can be inferred that this drug is an efficacious aid.) Further experience will determine the place that it should occupy in the treatment of infantile diarrhea with sulfonamide compounds.

Veinticinco de Mayo 2811.

THUMB AND FINGER SUCKING IN RELATION TO FEEDING IN EARLY INFANCY

ENA ROBERTS, R.N., B.S.

NEW YORK

Dr. David M. Levy, a child psychiatrist of New York City, concluded, after a series of clinical studies of children¹ and experiments with animals,² that babies suck their thumbs primarily because they do not get enough sucking from breast or bottle.

As a nurse in a Child Health Station of the Department of Health of the City of New York, I had a ready opportunity to test this conclusion. Furthermore, I was sufficiently well acquainted with the mothers who attended the station to be able to select those whose information was reliable. Even so it was necessary, after a preliminary study, to dismiss a number of informants because they were vague about changes in feeding schedules.

Only infants 7 to 8 months of age were selected, and data were collected concerning the feeding schedules followed during the first seven months. Fifteen known thumb suckers and fifteen known non thumb suckers constituted the two groups finally investigated.

Information was obtained as to (1) the type of feeding, breast or formula, (2) the number of feedings per twenty-four hours, (3) the changes in the feeding schedule, (4) the time per feeding and (5) the age of onset of thumb sucking. Questions concerning sucking of bottles containing fluids other than the regular feedings, such as water or orange juice, were not included. No infant in the group used a pacifier. Questions concerning sucking of toys or other objects that may have served the function of pacifiers were also not included. The data are therefore limited to the sucking time in relation to feeding only.

Through the courtesy of the New York City Department of Health, this article was submitted to Dr. David M. Levy as an interesting confirmation of his work on the same subject.

1. Levy, D. M.: Finger-Sucking and Accessory Movements in Early Infancy (An Etiologic Study), *Am. J. Psychiat.* 7:811-918, 1928.

2. Levy, D. M.: Experiments on the Sucking Reflex and Social Behavior in Dogs, *Am. J. Orthopsychiat.* 4:203-224, 1934; On Instinct-Satiation: An Experiment on the Pecking Behavior of Chickens, *J. Gen. Psychol.* 18:327-348, 1938.

It was found that in general non thumb suckers took a longer time for feeding than was taken by thumb suckers. There were, for example, no infants with a feeding time per day as short as thirty, forty or even sixty minutes at any time in the seven months in the former group, though there were periods of that length in the schedules of 9 infants who sucked their thumbs or fingers. On the other hand, instances of feeding time per day as long as ninety minutes occurred at some time during the seven months in the schedules of all infants who did not suck their thumb or fingers and in the schedules of only 8 of the 15 thumb suckers. If the incidence of long feeding time (ninety minutes or more) in the two groups is compared by units of one month it is seen that in the non-thumb-sucking group average feeding times of this length occurred throughout the seven months in 12 cases, whereas in the thumb-sucking group it occurred throughout the seven months in only 2 cases.

The distribution according to the average feeding time per day during the first seven months for the entire group of 30 infants and for the two subgroups was as follows:

Average Feeding Time, Min./24 Hr.	Number of Finger Suckers	Number of Non Finger Suckers	Percentage of Finger Suckers
Less than 40	3	0	100
40 to 69	5	0	100
70 to 99	5	5	50
100 to 129	2	7	22
130 and over	0	3	0

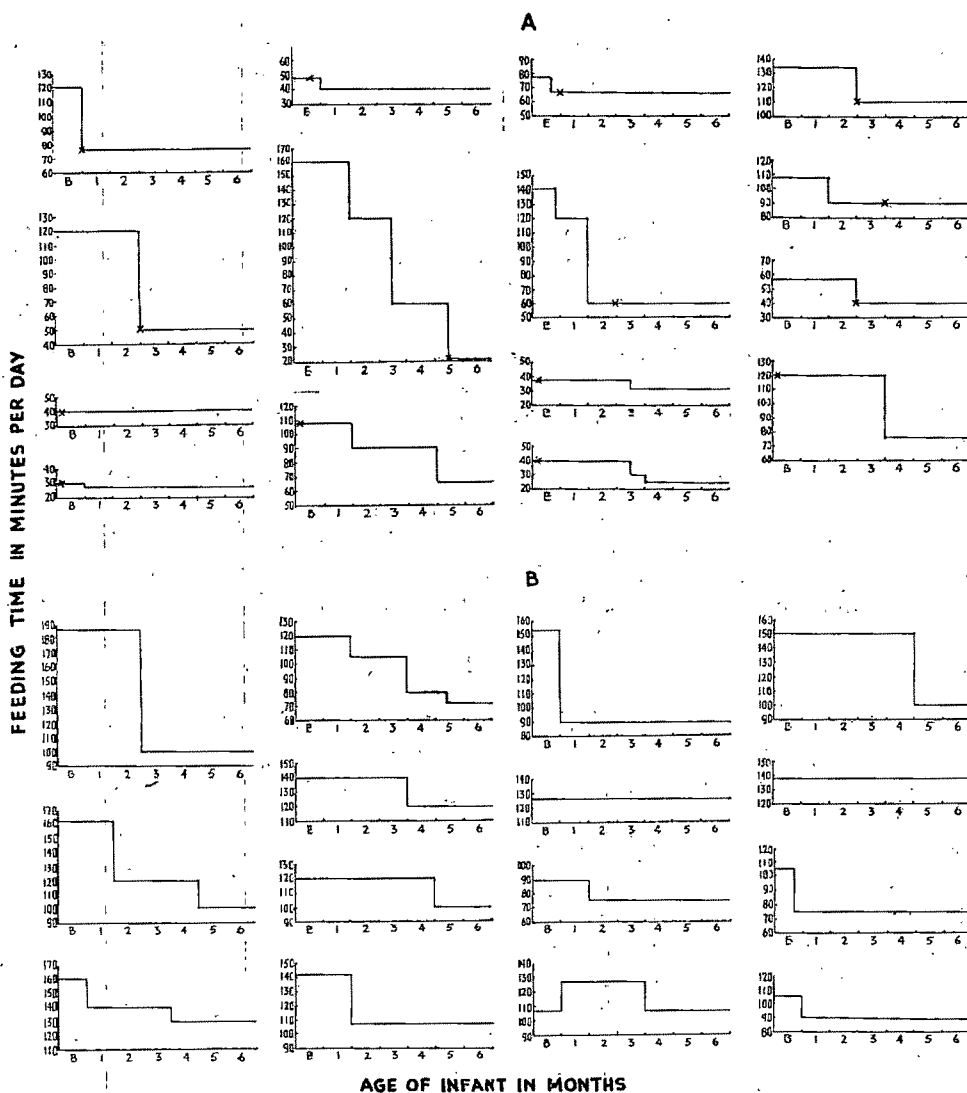
The relationship between the time spent in feeding and during each day thumb or finger sucking is clearly indicated. In the groups studied the percentage of thumb and finger suckers rose as the feeding time decreased and fell as the sucking time increased.

There is an important condition that is not revealed in the table, namely the onset of thumb and finger sucking after a sudden decrease in the feeding time. In 6 cases thumb and finger sucking began after a diminution of the feeding time occurred; in all but 1 of these, the onset occurred within a day to two weeks after the

change. This relationship may help to explain some instances of thumb and finger sucking in spite of long feeding time if the onset of the habit was preceded by much longer periods of feeding. In 3 cases of thumb sucking in which the feeding time averaged seventy-six, ninety and one hundred and ten minutes the period for feeding had previously averaged one hundred and twenty,

3 instances was the time reduced to less than eighty minutes per day.

Of 15 thumb and finger suckers, the onset of the habit occurred within the first month of life in 7, in the second month in 2, in the third month in 4, in the fourth month in 1 and in the fifth month in 1. In most of the infants the habit was established in the first two months. One



Individual graphs for 30 infants showing the average feeding time per day for each of the first seven months. A, charts for infants in whom the habit of thumb sucking developed. The time of onset of thumb sucking is indicated by an X. B, charts for infants who did not suck their thumbs or fingers.

one hundred and eight and one hundred and thirty-two minutes respectively. If the criterion of short feeding time in any period within the first seven months is combined with that of decrease in feeding time, only 2 cases of finger sucking are unaccounted for. It will be noted that in the non-finger-sucking group the decrease feeding time was gradual and that in only

case is interesting in that a gradual reduction in the feeding time occurred without thumb or finger sucking until the total time for feeding was reduced to twenty minutes per twenty-four hours.

This study clearly confirms Dr. Levy's observation that the amount of time spent in sucking is the primary determinant of the habit of sucking the thumb or fingers.

POISONING DUE TO LYE

VALUE OF BOKAY PROPHYLACTIC DILATION IN PREVENTION OF EARLY STRICTURES OF THE ESOPHAGUS

JOHN T. CROWE, M.D.

DURHAM, N. C.

Corrosive burns of the esophagus constitute one of the most difficult problems in pediatric practice.¹ Lye is used by poor people as a detergent and in the home manufacture of soap. These people do not realize until it is too late that a solution of lye which will "eat the stains from the boiling kettle" will have a much more dire effect on the oral or esophageal mucosa. As shown by the following series, in 86 per cent of the instances of the accidental use of lye the blame could be directly placed on an adult who carelessly left powdered lye or a solution of lye in a familiar container within the reach of a hungry, thirsty or curious child. In 5 per cent of the instances a child was given a drink from a glass not known to have contained lye, and in 9 per cent the patient took lye with suicidal intent.

At Duke Hospital from 1938 to 1943, 57 patients were treated for poisoning or for burns of the mouth, pharynx, trachea or esophagus due to lye. Fifty others had been reported on for the period from 1930 to 1937,² making a total of 107. In the present series 55 patients were poisoned with caustics (potassium hydroxide, sodium hydroxide or ammonium hydroxide), 1 with soap containing lye and 1 with household ammonia. The distribution of the patients according to age is shown in table 1. The 5 oldest patients drank the corrosive with unsuccessful suicidal intent.

From the Departments of Pediatrics and Otolaryngology, Duke University School of Medicine, and Duke Hospital.

1. Brown, H. W., and Kiser, G.: Epidemiology of Lye Poisoning in the United States, *Am. J. Pub. Health* **32**:822-830 (Aug.) 1942. Tucker, G.: Strictures of the Esophagus: Diagnosis and Treatment, *Laryngoscope* **41**:426-438 (June) 1931; Cicatricial Stenosis of the Esophagus, with Particular Reference to Treatment by Continuous String, Retrograde Bouginage with the Author's Bougie, *Ann. Otol., Rhin. & Laryng.* **33**:1180-1214 (Dec.) 1924. Taylor, H. M.: A Preliminary Survey of the Effect Which Lye Legislation Has Had on the Incidence of Esophageal Stricture, *ibid.* **44**:1157-1158 (Dec.) 1935. Jackson, C.: Cicatricial Stenosis Following the Swallowing of Caustic Alkalis, *J. A. M. A.* **77**:22-23 (July 2) 1921.

2. Martin, J. M., and Arena, J. M.: Lye Poisoning and Stricture of the Esophagus: A Report of Fifty Cases, *South. M. J.* **32**:286-290 (March) 1939.

TREATMENT

First Aid.—First aid for persons poisoned with lye should consist in slow oral administration of large amounts (500 cc., 1 pint) of vinegar (diluted with equal parts of water), orange, grapefruit or lemon juice or 2 per cent acetic acid as soon as possible. In this way alkali in the mouth, pharynx and esophagus will be neutralized without sufficient acid entering the stomach rapidly enough to cause vomiting. Then, 1 teaspoon of olive oil should be given every thirty minutes for six hours and every hour for the succeeding twenty-four hours. Removal of the caustic from the stomach by lavage is probably needless, because of the neutralization by gastric hydrochloric acid, and the resulting trauma may be dangerous. For two days after the first aid is

TABLE 1.—*Ages at Which the Patients Swallowed the Corrosive Substance*

Age, Yr.	Patients	
	Number	Percentage
1 to 2.....	36	63
2 to 5.....	15	26
5 to 10.....	1	2
10 to 20.....	3	5
Above 20.....	2	4

given, if liquid can be tolerated, the diet should consist of strained food and liquids every three hours, with $\frac{1}{2}$ teaspoon (about 2.5 cc.) of olive oil between feedings. During the next three days soft, semiliquid foods which are easily swallowed should be given. At the end of this period, after the edema and inflammation have subsided, the esophagus should be carefully and gently visualized by fluoroscopy while the patient is ingesting a small amount of a suspension of barium sulfate or, preferably, with a pharyngoscope (not an esophagoscope, which is dangerous to an esophagus damaged by lye) by a qualified esophagoscopist. In instances in which there is doubt, oral burns from caustic should be considered as presumptive evidence of esophageal burns and as indication enough for Bokay therapy, even though roentgenographic or pharyngoscopic evidence is lacking. If no lesion

are found or suspected, additional therapy is unnecessary, and the patient may be dismissed, with a warning to report to the hospital if dysphagia occurs. He also should be examined fluoroscopically while swallowing a small amount of a solution of barium sulfate every month for six months in order to detect secondary changes.

The early therapy received by 10 of 57 patients is not known. Thirty-two patients had received vinegar (amounts unknown), 9 had received lard, olive oil or liquid petrolatum and 2 had been given drugs (sulfathiazole or a sedative). The caustic had been removed from the stomachs of 4 patients by lavage.

Four of the patients had had esophageal dilation before admission to Duke Hospital but required gastrostomy and additional dilation. One of the patients had had the esophagus dilated for five days and was admitted with esophageal stenosis one hundred and thirty-five days later; 1 had had dilation every six months for three years but stenosis occurred thirteen years later; 1 had the esophagus dilated for two weeks and was admitted with a stricture ten weeks later, and the fourth had the tube dilated for four weeks, beginning four weeks after the lye had been swallowed, and was admitted later with esophageal stenosis.

Six children in this series were seen at Duke Hospital thirty to one hundred and twenty minutes after the accident and were treated in the dispensary with acid and oil only. Four of them are known to have had no subsequent symptoms of stricture, and 2 did not return for further diagnosis or treatment.

Bokay Prophylactic Therapy.—If the presence of oral burns or the conditions revealed by fluoroscopy or pharyngoscopy indicate that the esophagus has been damaged, even slightly, an eyeless (Bokay) catheter,³ size 10 to 30 (French), which has been filled with lead shot or mercury, tied off at the open end and wet with water or with K-Y lubricating jelly (to avoid the possibility of lipid pneumonia from the use of greasy lubricants) should be gently passed down the child's esophagus (not more than 2 cm. [1 inch] entering the stomach) and left in place for five minutes, once daily,⁴ starting on the third day after the child swallows the lye, or as near that time as possible. The catheter should not be forced but allowed to pass merely by weight of the shot or mercury contained in it.

3. Bokay catheters can be obtained from Murray-Baugartner Surgical Instrument Co., 5 and 7 West Chase Street, Baltimore, or the eye of an ordinary catheter can be closed at any tire-vulcanizing shop.

4. Bokay, J.: *Salzer's Treatment of Lye Poisoning*, Wien. klin. Wchnschr. **37**:282-285 (March 30) 1942.

5. Vi, V.: *Prophylaxis of Lye Accidents*, München. Wchnschr. **70**:772 (June 15) 1923.

This will give adequate force to pass the usual developing stricture without rupturing the esophagus if it should fall into a sacculation. During the first few days the size of the catheter used should be increased until difficulty is encountered in passing it. From the third to the tenth week the largest possible catheter should be passed once daily and kept in place for ten to thirty minutes. The catheter should be introduced twice a week for the next month and then once a week for at least three months; then the interval can be lengthened to suit the patient's condition. I do not mean that the treatment should not be individualized, but the procedure outlined is the safest. The patient should always be warned that the success of the treatment depends on early and continued prophylactic dilation, tedious and uncomfortable though it is.

Unfortunately, only 13 of the patients (23 per cent) were seen in a sufficiently early stage of esophageal damage so that Bokay prophylactic therapy could be used. In the 9 patients for whom Bokay therapy was adequate no strictures of the esophagus occurred (table 3). For 4 children, however, owing to failure of the families to cooperate, the treatment at home was not sufficiently prolonged, and strictures developed, necessitating a second admission to the hospital for gastrostomy and bougienage. It is important to be sure the dilator is completely into the stomach (but not more than 2 cm.), even if it is necessary to use fluoroscopy. In 1 of the patients whose esophagus was not thoroughly dilated a stricture developed at the cardiac orifice while the patient was under treatment. After checking back it was found that the catheter was not long enough to get into the stomach and thus to dilate this low stricture, though two higher strictures were dilated adequately. The average time spent in the hospital by the 9 patients for whom Bokay therapy was successful was twenty-five days, costing \$160 per patient at \$5.40 per day.

Bougienage.—Forty-four of the patients (77 per cent) had esophageal strictures sufficiently severe at the time of admission to the hospital to require bougienage. They did not arrive at the hospital early enough to be given Bokay therapy (not until an average of fifty-six days⁵ after the accident). Four others had inadequate Bokay treatment (table 2) and required more radical procedures. If a partial stricture has formed and Bokay dilation cannot be used, a lead-weighted silk thread, to which bougies can subsequently be attached, should be given to the

5. Omitting 5 patients for whom the intervals between the swallowing of lye and the development of the esophageal stricture were three, four, eleven and one-half, twenty and twenty-four years.

patient on repeated occasions until the shot passes into the stomach. This simple but difficult procedure, if done as soon as Bokay therapy is found impossible, will save time and occasionally a life.

TABLE 2.—Records of Thirteen Patients for Whom Prophylactic Bokay Therapy Was Used

Patient No.	Interval Between Swallowing of Lye and Admission to Hospital, Days	Total Days in Hospital	Stricture	Bokay Therapy Continued at Home	Condition (When Last Seen, Either in the Outpatient Clinic or at Discharge From the Hospital)
2	1	35	No	Yes	Good
3	1 (second admission)	26 (76)†	No Yes	No	Physician could not dilate esophagus because he "had no equipment for it"; gastrostomy and retrograde dilatation done
22	5 (second admission)	85 (63)†	No Yes	No	Gastrostomy one and a half months after first discharge, due to stenosis
26	1	15	No	No	Condition good at discharge
32	6	24	No	No	Condition good twenty-four months after discharge
37	1	20	No	No	Good at discharge
40	1 (second admission)	0 (87)†	No Yes	Irregularly	Gastrostomy because patient was not brought to outpatient clinic for regular dilations
42	7 (second admission)	0 (101)†	No Yes	Irregularly	Gastrostomy because patient not treated regularly
46	46	12	Yes	Yes	Good
49	28	9	No	Yes	Good
51	4	48	No	Yes	Good
52	2	22	No	Yes	Good
54	1	40	No	Yes	Good

The average stay in the hospital was twenty-five days for patients receiving Bokay therapy without gastrostomy and fifty-one days for patients having secondary gastrostomy.

* All 13 patients on admission had fluoroscopic or esophagosopic evidence of having swallowed caustic, and 1 had a slight stricture. All except 1 child (no. 32) had had vinegar as the first treatment; no. 32 had water only.

† Second figure indicates duration of the second admission, for secondary gastrostomy.

In half of the patients the strictures were just below the cricopharyngeus muscle, in the upper third of the esophagus, possibly because of spasm of the esophagus when the corrosive irritated it (table 3). All of the patients with strictures required one of the following types of treatment: (1) peroral esophagosopic bougienage, (2) retrograde bougienage through an artificial gastric fistula or (3) peroral bougienage with a silk thread used as a guide, procedures which involve long hospitalization, inconvenience, expense and the possibility of death from surgical causes. The 48 patients spent an average of fifty-six days in the hospital, a total of two thousand six hundred and seventy-five days. The maximum number of days of hospitalization was

two hundred and twenty-three; the minimum was one day, and the average per admission was thirty-four days. As the daily cost for hospitalization is \$6.40, the average expense per patient for hospitalization was \$358, a total of \$17,120 for the 48 patients with esophageal strictures. This is a high penalty to pay for carelessness in leaving an everyday household article within the reach of curious children. Duke Hospital has had to bear the major part of the expense, as 85 per cent of the patients were unable to pay the minimum rate for hospitalization and required assistance from some welfare organization, Duke Hospital or the Duke endowment fund to finance the protracted treatment.

PROGNOSIS

Trousseau's statement that "sooner or later all cases of esophageal stricture die of the bougie" has little basis today. All 9 of the patients for whom the Bokay therapy was adequate (table 3) escaped esophageal stricture, and the children were in good condition six months to four years after the accident. Strictures developed in 4 patients for whom the Bokay treatment was not continued at home and in 44 children who did not have Bokay treatment. Four of these 48 patients died, a mortality of 8 per cent. Two of the 4 patients died with esophagotracheal fistula, 1 with postoperative empyema and 1 with mediastinitis secondary to infection of the gastrostomy wound.

One of the patients had an esophagotracheal fistula at the time of admission to the hospital

TABLE 3.—Location of Strictures of the Esophagus Caused by Lye

Location	Number of Patients *	Percentage
Upper third.....	16	43
Middle third.....	7	19
Lower third.....	7	19
Upper and middle third.....	1	3
Upper and lower third.....	2	5
Middle and lower third.....	4	11
	37	

* Five patients who required gastrostomy but for whom the location of the stricture is not known are not included in this table.

and died the same day. In the other patient the fistula developed because the esophagus, larynx and trachea had been burned severely; the child died after a long and stormy course. The patient who died as a result of operative injury had complete stenosis of the esophagus, and the latter was perforated in attempted dilation through the esophagoscope.

Malignant degeneration in the scar of a burn of the esophagus due to lye, mentioned by Vinson,⁶ did not occur in any patient in this series.

SUMMARY

Fifty-seven cases of ingestion of caustic alkali were analyzed.

Too many infants and children are poisoned with lye because it is carelessly left within their reach. The first aid given is generally poor because it is incomplete.

Patients with early poisoning due to lye can be saved the ordeal, expense and dangers of

secondary stenosis of the esophagus by the use of Bokay prophylactic esophageal dilation. This treatment should be used for every patient who has swallowed alkali in any form, unless there is definite pharyngoscopic proof that the esophagus is undamaged. However, the treatment must be complete to be successful; too many patients are pronounced cured after receiving inadequate first aid.

Delay in treatment necessitates more drastic measures and is accompanied with 8 per cent mortality (as seen in this series), but careful attention to the prevention of secondary stricture and long-continued dilation produce good results in the other 92 per cent of the patients.

Duke University.

6. Vinson, P. P.: Cicatricial (Benign) Stricture of the Esophagus: Tabulated Report of One Hundred and Eighty-Six Cases, *Ann. Otol., Rhin. & Laryng.* **36**: 40-56 (March) 1927.

STUDY OF THE PERSONALITIES OF CHILDREN WITH DIABETES

WINIFRED C. LOUGHLIN, M.D.,* AND HERMAN O. MOSENTHAL, M.D.

NEW YORK

The statement that children with diabetes mellitus are like other children in personality before the onset of the disease is made with caution, because it may be argued that diabetes is an endocrinopathy and that such a condition is often accompanied with disturbances of personality. However, so many children with diabetes remain normal that we can only say that the changes in others are the result of the disease itself. The abnormal personality that not infrequently develops with juvenile diabetes is worthy of discussion and investigation. Experiences in dealing with a large number of diabetic children for a few years in a summer camp conducted by the New York Diabetes Association were reviewed, and certain facts and common factors presented themselves.

During a recent summer camping period 114 children were seen, about an equal number of boys and girls, ranging in age from 6 to 18 years. The group was unselected except for the exclusion of children with contagious diseases or known delinquency. They were mainly children from greater New York, and most of them attended clinics in that city. A few were being cared for by private physicians. The group was representative of previous ones at the camp, and many of the children were "old campers."

About three fifths of the children maintained normality in all respects. Normality may be briefly defined as possession of a sense of security, acceptance by a group, interest in the activities of the group, a healthy attitude toward bodily functions without preoccupation by them, absence of the urgent need for indulgence at a given moment and ability to endure a moderate amount of deprivation. The data for normal children closely approximated those for children in the abnormal group. The groups were equally distributed as to sex. The average duration of the diabetic condition in the normal children (4.08 years) was similar to the average for the entire group (4.3 years) and to that for the children classified as abnormal (4.15 years).

From the New York Diabetes Association, Inc.

*Resident Physician and Director, 1941 and 1942, Camp Nyda (summer camp for diabetic children, conducted by the New York Diabetes Association, Inc.).

The average age of the normal children was 13.3 years, compared with 13 years for the whole group and 12.6 years for the abnormal children. The average age at the onset of diabetes for the normal children was 9.2 years, for the entire group 8.5 years and for the aberrant children 7.7 years. The normal and the abnormal group and the entire series included approximately the same percentages of children with excellent control of the diabetic condition, 53, 50 and 51 per cent respectively. Ketosis occurred frequently in 18 per cent of the children of the entire series and in only 12 per cent of those who were emotionally well adjusted, while the incidence in the abnormal children was 23 per cent, twice that in the normal children. From these data only two important facts stand out: First, in the children with abnormalities of personality the onset of diabetes occurred one and a half years earlier than in the children with normal personalities, and, second, twice as many of the children with abnormalities had frequent ketosis. Perhaps the first may be a cause of disorders of personality and the second a result.

That most children with diabetes appear to be normal is a credit to themselves, to their parents and to the clinic or doctor responsible for their supervision. The parents, and especially the mother, are subjected to the urgent need of the diabetic child for care, his excessive dependency and an intense conscious or unconscious desire for mothering. The parent who can respond to all of these and yet temper them with moderation and unobtrusiveness is an asset to the child. The child is indeed fortunate who is treated at a clinic or by a doctor who can control the diabetic condition without instilling ever present consciousness of calories and carbohydrates, of urinalyses and of injections of insulin.

About two fifths of the children observed at the camp were thought to be abnormal in one or more respects. The abnormalities ranged from true neurotic states to simple disturbances of personality. Such difficulties may be expected in persons with a chronic illness like diabetes. A child with diabetes is pitted against a force that does not yield. "Bringing the problem to consciousness," the time-worn remedy for a neurosis

does not help. The problems inherent in the diabetic condition remain, insoluble, incurable, and if the child cannot accept the actualities he is lost. A reaction of defeat and discouragement sets in, with a consequent sense of helplessness. At this point, if the parent suffers from the same sense of helplessness the die is doubly cast.

Comfort and avoidance of pain, two fundamental characteristics of the normal condition, are repeatedly denied the diabetic child. Every day he must recall that he cannot eat this or drink that; every day he must give himself insulin hypodermically. The normal ability to perform the excretory functions without preoccupation is also denied him. He must save specimens of urine; frequently he is made to time his voiding in relation to meals, and he is occasionally plagued by polyuria. One diabetic patient proudly announced that he could "guess" the percentage of sugar in his urine by its color at voiding! A diabetic adult on a cruise insisted that a fellow voyager come to his cabin for a display of his urine-testing equipment. The person with diabetes frequently forgets that no one else except another person with diabetes is interested in urinalysis.

The child who is different from his playfellows is a good candidate for a neurosis. A few children at the camp, even though among others with diabetes, were so unconditioned to group play that they frequently begged off from or interrupted games, theatrical performances or other juvenile activities with various somatic complaints. The complaints were of a nature usually heard only from adults with ingrained neuroses (for example, headache, backache, fatigue or palpitation).

A 10 year old boy at the camp for the first time presented the picture of an athletically active and normally aggressive child; he thought little of his diabetic condition, albeit it was always well controlled. After being subjected to the camp's elementary "lectures" on diabetes and routine urinalyses and to the other children's talk of diets, he became in the course of the following year increasingly more preoccupied with his disease; he began to question his mother's and his doctor's management and to suggest more frequent testing of urine. Instances like this have made us place less emphasis on diabetes at the camp and have made us decrease the number of urinalyses per day from four to two.

Aberrations of personality occurring in the young and adolescent children observed were of a few clearcut categories including the "aggressive," the "retiring," the "devil-may-care," the

"immature," and the "escapist" type. All these disorders, of course, may result from the fact that diabetic children have a "feeling of difference."

Aggressive diabetic children may be like ordinary superior children who have to be best in games, best in school and best in health. This attitude is constructive. However, a few of these children become aggressive over unimportant things; they quarrel over minor events and give lectures to their fellows on scholastic topics or about matters that are common knowledge. One boy, who was really superior, memorized long poems and recited them breathlessly to any one who was polite enough to listen and held the impolite with the "ancient mariner's" grip. Another child, who was average, stated her belief in her superiority by saying that her father told her that Jewish children were brighter than others and that diabetic children were brighter than normal ones, leaving the evident conclusion to be made.

Retiring diabetic children are apt to be overshy and ever mute. However, they do not seem to have the excessive sensitiveness and awareness so often associated with overshyness. One boy, seen in private practice, gave the impression of reticence until talked to away from his father, a dynamic business man who had taken over complete control of the boy's diabetic regimen. These children give the impression of "numbness."

The "devil-may-care" reaction is dangerous. Children who exhibit this reaction are characterized by overwhelming hopelessness; they generally eat anything and everything and eventually become escapists. An adolescent boy who wanted to obtain a pilot's license reacted with indifference when the danger of hypoglycemia was recalled to him. The boy had been completely out of control for four years and had deceived his parents and his doctor. He had failed to grow, and his height was 5 inches (13 cm.) less than the average for his age. His ordinary mode of conversation was one of untiring but pleasant flippancy. Another adolescent boy, who had frequent and severe episodes of ketosis, stated that he was given the syringe for his injection by his mother and sent into a closed room to administer it to himself; his mother could not bear the sight of the procedure. When he became "tired of it all," he ejected the insulin into the air and emerged from the room, triumphant in having deceived his mother and his doctor. This boy too was unvaryingly flippant.

The reactions of immature diabetic children are pleasant but infantile; at the age of 11 or 12 years they exhibit the judgments and reactions

of a child of 6 or 7 years. These children are frequently undersized and poorly controlled. Personality disorders of this type probably have an organic basis.

The escapist is the child who uses ketosis as a refuge from the unpleasantness of home or school or even as a refuge from the "struggle" against poorly managed diabetes itself. About one third of the children who had frequent episodes of ketosis came from homes broken by divorce, separation or widowhood, homes from which the mother was away all day and in which meals were consequently haphazard. Most of these children frankly stated that they liked the hospital better than home. The ordinary escapes of an unhappy child might be viewed as innocuous when compared with the devastating effects of the escape which is open to the unhappy diabetic child.

Normal adolescent children have many problems commensurate with their changing status. Diabetic adolescent children may be overwhelmed by their difficulties. They are subject to all the forms of adolescent flights of fancy, and inevitably they can satisfy but a few of them. They are thrown in with school fellows who make the cafeteria and the soda fountain their meeting place. If they do not become indulgent, they may become asocial. Undersized diabetic children may well feel inferior during this period in which rapid growth and maturation are normal. When they come to apply their maturing judgment to plans for a life work, they must do so with much more foresight than their normal contemporaries need to use. They must further bear in mind the hereditary possibilities of the disease, the life span associated with it and the complications now thought of as part of diabetes. It may be that at this age they begin to think that nature has played a monstrous physiologic trick on them. They may demand compensation for the handicaps, and this may result in a drive toward normality in all other respects or it may warp the personality.

Oddly enough, fear of the embarrassment and the danger of hypoglycemic reactions does not play a prominent role in the makeup of young persons with diabetes. This may be because they have little or no memory of the episodes, due to the attendant physiologic decortication.

It is difficult to formulate rules for the prevention of disturbances of personality in young persons with diabetes. Each case must be handled individually, as in any other disorder, but a few simple guideposts stand out. With

diet-insulin therapy for diabetes it is no longer necessary to make the child too conscious of food. The day of weighing food is over and measuring resembles the normal everyday way of dispensing food even in the home. The appreciation of only a few simple values for substitutions is all that is essential for successful dietary management. The problem of weaning from candy, ice cream and cake is a more difficult one; possession of these foods is almost the right of a child. The elimination should be sudden and complete, without recourse to substitutes. Self administration of insulin should be started in the hospital or the clinic and continued at home, even if the mother wants to assume the responsibility. When good control is attained, urinalyses should be less and less frequent, the management varying, of course, with the estimate of the child's dependability. Every urinary examination and the translation of the results into adjustment of the diet and the insulin therapy is a serious matter, and if the procedure is carried out incessantly it is prone to lead to irritability and even desperation. If urinalyses are distracting a child from normal pursuits or preoccupying him too much and yet are essential, let the mother become the tester. A mother may seek, with the best of intentions, to compensate her child for his illness by urging him too strongly in other pursuits. This, too, must be discouraged. Children who are too frequently in the hospital should be investigated for maladjustment. When children with diabetes are approaching adulthood they should be encouraged to discuss their problems and their future. If they seem unhappy, it does not really help to reassure them robustly that they are like any one else in adolescence. It may be a mistake to conclude that because modern therapy has made them physically indistinguishable from their neighbors diabetic persons are of the average emotional coloring. Finally, it may be advisable for the physician periodically to spend a half-hour in conversation with each child who has diabetes to find out how he feels about himself, his fellows and his environment. The patient's personality may be disclosed only then, even though he has made routine visits for control of diabetes for several months or years. The early recognition and treatment of emotional conflicts and behavioral disorders in children with diabetes by an alert physician might go a long way toward evolving better adjusted diabetic adults.

889 Lexington Avenue.

BASAL BLOOD PRESSURE AND PULSE RATE IN ADOLESCENTS

NATHAN W. SHOCK, Ph.D.*

BERKELEY, CALIF.

Although measurements of the blood pressures of large populations of normal adults have been reported and the limits of normal variation have been fairly well established,¹ relatively few measurements have been made for developing adolescents.² Pulse rates of untold thousands of high school children have been counted under unknown conditions of rest or exercise, but the information available on changes in the basal pulse rate with age during the adolescent period is scanty.³ This report presents the results of repeated measurements of pulse rate and blood pressure taken at intervals of six months for the same persons (children aged 11.5 to 17.5 years) under basal conditions over a period of six years.

From the Institute of Child Welfare and the Division of Physiology, University of California.

*Now Senior Psychophysicologist, United States Public Health Service, National Institute of Health, Unit on Gerontology, Bethesda, Md., and Visiting Physiologist, Baltimore City Hospitals, Baltimore.

1. (a) Medical Impairment Study (1929), New York, Actuarial Society of America, 1931. (b) Alvarez, W. C.: Blood Pressures in Fifteen Thousand University Freshmen, *Arch. Int. Med.* **32**:17-30 (July) 1923. Alvarez, W. C., and Stanley, L. L.: Blood Pressure in Six Thousand Prisoners and Four Hundred Prison Guards, *ibid.* **46**:17-39 (July) 1930. (c) Hunter, R. G.: A Statistical Study of Blood Pressure, *Am. Inst. Actuaries* **13**:203 (Nov.) 1924. (d) Lewis, W. H.: Changes with Age in the Blood Pressures in Adult Man, *Am. J. Physiol.* **122**:491-505 (May) 1938. (e) Robinson, S. C., and Brucer, M.: Range of Normal Blood Pressure: A Statistical and Clinical Study of 11,383 Persons, *Arch. Int. Med.* **64**:409-444 (Sept.) 1939.

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3. (a) Robinson, S.: Experimental Studies of Physical Fitness in Relation to Age, *Arbeitsphysiol.* **10**:251-323, 1938. (b) Sutliff, W. D., and Holt, E.: The Age Curve of Pulse Rate Under Basal Conditions, *Arch. Int. Med.* **35**:224-241 (Feb.) 1925.

SUBJECTS AND PROCEDURE

The subjects for the cumulative study were 50 girls and 50 boys, chosen for the University of California Adolescent Growth Study from five elementary schools of Oakland, Calif. Since repeated testing of the same children was contemplated, selection of the subjects was based on the likelihood of their permanent residence and the cooperation shown by their parents. When first tested the children had a mean age of 11.87 years (with a standard deviation of 0.5 year).⁴ The children of this group were retested at intervals of six months.

Additional groups of 50 girls and 50 boys were chosen from the same school population, and each child was given a single pair of tests. The boys were designated group A and the girls, group B. These children had a mean age of 16.0 ± 0.2 years at the time they were tested.

Similar tests were made for a group of 20 men who were medical students aged 23.9 ± 0.7 years⁵ and 15 women students aged 23.2 ± 0.7 years. Values were also obtained for 20 men aged 32.5 ± 0.3 years and 17 women aged 33.4 ± 1.2 years.

On the morning of each test, the subject was brought by automobile to the laboratory, without breakfast. After the height and weight were measured, a standard 12.5 cm. cuff with leather backing was attached to the left arm. After determinations of blood pressure (by the use of a calibrated mercury manometer) and pulse rate were made with the subject in the standing position, he lay down on a cot for twenty minutes, during which time three additional measurements of pulse rate and blood pressure were made. Determinations of basal metabolic rate were then made by the open circuit method, for periods of eight minutes. Measurements of blood pressure and pulse rate were made at the close of each of three tests of basal metabolism. In the present report the average of the measurements taken at the end of the first and second tests of basal metabolism are presented.⁶ The average of four measurements (two on each day) was computed for each subject and used in the present analysis.

4. A more detailed description of the children of this study is given by Jones (Jones, H. E.: The Adolescent Growth Study: I. Principles and Methods, *I. Consult. Psychol.* **3**:157-159, 1939; II. Procedures, *ibid.* **3**:177-180, 1939).

5. In this paper ± 1 standard error is reported for all mean values.

6. The measurements made at the end of the third test were excluded because in many subjects these values were higher than the ones taken at the end of the second period. Ogden and Shock (Ogden, E., and Shock, N. W.: The Rate of Stabilization of Systolic Blood Pressure Following Adoption of the Supine Posture, *Quart. J. Exper. Physiol.* **28**:341-348 [Dec.] 1938) have shown that in adults twenty minutes' rest in the supine position affords ample time for stabilization of systolic blood pressure.

Pulse rates were counted for a full minute. Measurements of blood pressure were made by the auscultatory technic; systolic pressures were recorded at the first sound and diastolic pressures at the first muffling of the sound (fourth sound of Korotkow).

RESULTS

Reliability of Measurements.—From the correlation between observations made at the end of the first and second tests of metabolism (about ten minutes apart) it was found that the probable error of a single measurement of systolic blood pressure made under these conditions was 1.5 mm. for the values for boys and 1.8 mm. for the values for girls. The probable error of the values for diastolic pressures was 1.8 mm. for boys and 2.2 mm. for girls. The probable error of estimates of pulse rate was 1.8 beats per minute for

of the values for systolic blood pressure was 1.91 mm. for boys and 2.45 mm. for girls. For diastolic blood pressure the probable error of measurement was 2.2 mm. for boys and 2.5 mm. for girls. The probable error of measurement for pulse rate was 1.7 beats per minute for boys and 2.1 beats per minute for girls. Examination of the probable errors of measurement leads to the conclusion that fluctuations in basal pulse rate and blood pressure are almost as great during intervals of ten minutes as they are during periods of twenty-four hours.

Age Norms for Blood Pressure and Pulse Rate.—From the average of the four measurements made on two days distributions for each of the variables according to the ages of the

Table of Average Values for Basal Pulse Rate and Blood Pressure in Adolescent Children

Age, Years	Basal Pulse Rate, Beats per Min.		Basal Blood Pressure, Mm. Hg												Pulse *							
			Systolic				Diastolic															
			Boys		Girls		Boys		Girls		Boys		Girls									
	Mean	σ†	Mean	σ	Mean	σ	Mean	σ	Mean	σ	Mean	σ	Mean	σ	Mean	σ						
11.5	67.5	6.6	74.1	11.7	102.7	6.7	106.6	9.6	98.7	5.3	72.9	6.5	34.7	5.3	34.1	7.5						
12.0	69.5	8.1	71.4	7.8	104.2	7.2	103.8	7.3	71.1	5.2	71.3	6.9	33.8	4.8	33.7	5.1						
12.5	66.8	6.6	69.2	6.0	104.9	6.7	105.9	7.0	39.8	4.8	71.6	7.2	35.4	5.9	34.8	5.3						
13.0	65.9	6.0	67.8	8.0	106.0	6.1	105.3	7.0	69.6	5.2	69.8	5.2	37.1	5.4	36.3	5.4						
13.5	66.2	5.5	69.6	8.1	107.7	6.7	107.5	7.0	39.0	5.3	68.3	6.1	39.3	6.1	39.1	6.9						
14.0	67.1	7.0	68.3	6.9	110.7	8.6	108.0	7.0	36.5	4.8	68.0	6.3	42.8	6.3	40.6	6.5						
14.5	66.0	6.1	67.6	6.9	110.7	6.6	106.4	4.6	38.3	5.1	67.0	4.8	43.3	5.1	40.1	5.4						
15.0	65.2	5.5	67.3	8.6	110.4	7.0	105.4	6.7	39.3	4.8	68.3	5.4	42.1	6.5	38.4	5.5						
15.5	63.1	6.4	66.7	8.2	111.1	6.2	104.1	5.4	70.3	5.1	68.1	5.1	41.5	6.2	36.9	6.2						
16.0	61.6	6.5	65.8	7.6	112.4	7.1	106.8	9.3	71.3	5.5	69.4	5.4	41.7	6.8	37.5	6.7						
16.0 †	61.5	7.9	66.7	8.3	113.3	10.0	104.3	4.8	72.0	6.9	75.8	7.5	42.0	7.1	37.2	4.0						
16.5	60.8	6.3	66.4	8.4	111.1	7.0	104.9	4.8	70.3	4.9	67.8	5.9	41.2	5.5	37.9	6.5						
17.0	58.6	4.8	64.1	6.9	114.7	7.0	107.0	8.0	71.9	5.1	69.1	7.8	43.4	6.8	38.6	6.7						
17.5	58.7	6.8	63.7	6.3	114.4	6.2	106.4	6.4	71.0	4.6	68.7	4.5	43.8	6.8	37.1	5.6						
24 §	61.0	7.0	69.2	8.4	112.1	4.5	108.0	5.4	75.0	5.5	72.3	6.1	37.8	5.8	36.2	6.2						
30 §	59.3	6.1	64.8	8.5	114.4	6.9	110.0	5.1	30.0	7.0	75.8	7.5	34.8	4.4	34.8	5.0						

* Pulse pressures were calculated from each individual set of measurements.

† σ represents the standard deviation of the distribution.

‡ Values for the control group of fifty 16 year old children who were tested only once.

§ Measurements for different groups of subjects.

boys and 2.5 for girls. The error of estimate of determinations of the blood pressure of adolescent children is thus of the same order of magnitude as that previously reported for determinations for adults.⁷

Correlations between measurements made on two successive days were also calculated and served to give an estimate of the day to day variability of blood pressure and pulse rate. The probable error of measurements on two successive days was calculated from the standard deviation of the distribution of the measurements and their correlation.⁸ The probable error of measurement

subjects were prepared. Age classes were chosen so that the midpoints fell at years and half years. Because of unavoidable irregularities in the schedules of tests for some children the number of subjects in each age group varies between 50 and 30 except in the groups at 11.5 and 17.5 years, in which the number falls to 16. If two tests on the same child fell within the same age category, only the test nearest the midpoint of the category was used in the calculation. The results are summarized in the accompanying table.

Chart 1 shows the average pulse rates (beats per minute) of boys and girls between the ages of 11.5 and 17.5 years. The length of the vertical line through each point indicates the value for plus and minus one standard error of the mean. Points A and B indicate the mean values for the control groups of 16 year old boys and girls respectively. The values at the ages of 24 and 33 years were

7. Shock, N. W., and Ogden, E.: The Probable Error of Blood Pressure Measurements, *Quart. J. Exper. Physiol.* **29**:49-62 (March) 1935.

8. The formula used was $P.E. = 0.6745 \frac{\sigma_1 + \sigma_2}{\sqrt{1 - r}}$. Garrett, H. E.: *Statistics in Psychology and Education*, ed. 2, New York, Longmans, Green & Co., 1937.

obtained from measurement of different subjects, as described in a previous paragraph. Although the average pulse rate of girls is always greater than that of boys, the difference is not statistically significant.⁹ However, the decrease in pulse rate during adolescence is statistically significant. In boys the average pulse rate falls from 59 beats per minute at age 12 to 59 at 17.5. In girls the decrease is from 72 to 64 beats per minute during the same period.

Chart 2 shows the average systolic blood pressures for adolescent boys and girls. There is no difference between the systolic blood pressures of boys and of girls under 3½ years of age. Between the ages of 11½ and 13½ the average blood pressure rises from 103 to 108 mm. in children of both sexes. After the age of

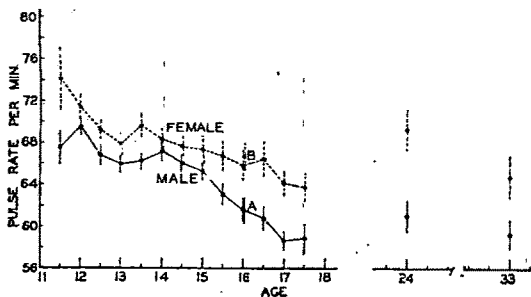


Chart 1.—Curves for average basal pulse rates of boys and girls tested every six months between the ages of 11.5 and 17.5 years. Connected points were obtained from tests on the same children as they matured. Points shown at ages 24 and 33 years were obtained from tests on other subjects (see text). Points marked A and B are average values for 50 additional boys and 50 additional girls aged 16 years who were tested for the first time at this age. The length of the vertical line through each point indicates the value of one standard error of the mean. The solid line represents the values for boys; the broken line, those for girls.

13½ the systolic pressure of boys continues to rise, reaching a value of 114 mm. when the boys

9. The fact that the average pulse rate for girls is greater than that for boys at all ages cannot be used as an argument to establish the validity of the sex difference observed in this study, because, since the same children were measured at each age level, any chance sampling difference present at the first testing was maintained. However, different subjects were measured in the 24 and 33 year age groups; so the higher pulse rates for females than males offers some evidence of a true difference. Other investigators have also reported higher pulse rates for women than for men (Bzwerman, W. G., and Brett, J. H.: *Pulse Rates*, *Quart. Rev. Biol.* 16:90-99 [March] 1941; also footnotes 1 a and 3 b). Although pulse rate is negatively correlated with body size (Mautner, H.; Luisada, A., and Weisz, L.: *Physiological Tachycardia in the Young*, *Arch. Pediat.* 58: 562-569 [Sept.] 1941), girls do not show slower pulse rates than boys between the ages of 11.5 and 14.5 years, when they are on the average taller and heavier than (chart 1).

are 17.5 years old, while that of girls drops slightly, reaching a minimum of 104 mm. when they are 15.5 years of age. In girls beyond this age there is a slight rise in pressure, to 106 mm. at 17.5 years. In this physiologic characteristic a sex difference develops during adolescence and seems to persist throughout life.

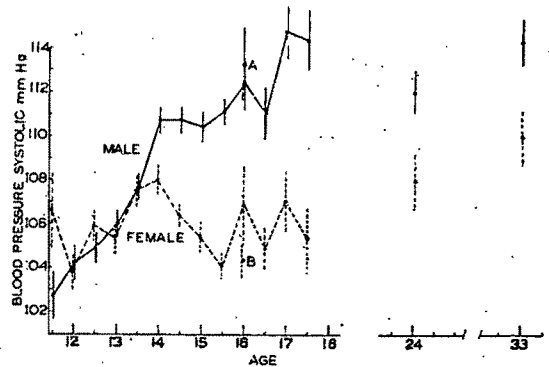


Chart 2.—Curves for average systolic blood pressures of boys and girls between the ages of 11.5 and 17.5 years and for men and women at 24 and 33 years.

Changes in the diastolic blood pressure with age are shown in chart 3. Between the ages of 12 and 14.5 years there is a downward trend in diastolic pressure of both boys and girls, but at 14.5 the average diastolic pressure begins to rise again, so that at 17.5 the values are almost the same as they were at 12 years. This rise in diastolic pressure seems to continue at least to age 35. There is no statistically significant difference between the diastolic pressures of boys and of girls during adolescence.

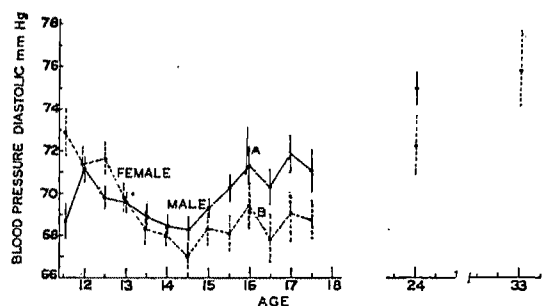


Chart 3.—Curves for average diastolic blood pressures of boys and girls between the ages of 11.5 and 17.5 years and for men at the age of 24 and women at the ages of 24 and 33.

Chart 4 shows the development of a sex difference in pulse pressure (systolic pressure minus diastolic pressure) in adolescent children. The average pulse pressure rises from 34 mm. at age 11.5 to 39 mm. at age 13.5 in both sexes. Beyond this age the pulse pressure of boys continues to rise, while that of girls falls, resulting in a sig-

nificant sex difference between the ages of 15 and 17.5 years. It is interesting to note that this sex difference was not noted in adults tested and that the values for pulse pressure were at preadolescent levels.

Effect of Early or Late Sexual Maturity on Basal Cardiovascular Measures.—Inadequacies and limitations of chronologic age as an index of maturity have long been recognized, but for clinical use a successful substitute is yet to be devised. Other indexes of physiologic maturity have been proposed, such as ossification of hand,

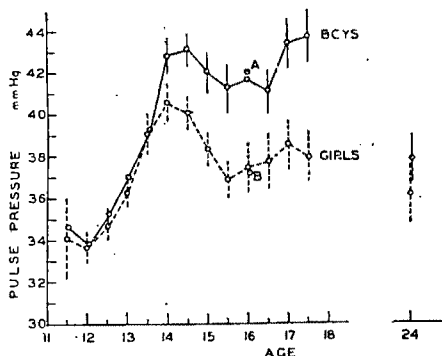


Chart 4.—Curves for average pulse pressures of boys and girls between the ages of 11.5 and 17.5 years and for men and women at 24 years.

wrist, or knee,¹⁰ menarche¹¹ or age of maximum rate of growth.¹² Of these age at menarche has perhaps been pursued with greatest enthusiasm. Although there is occasion for grave doubt of the advisability of basing estimates of maturity on a physiologic event subject to so many variables both within and without the organism, it

10. (a) Flory, C. D.: *Osseous Development in the Hand as an Index of Skeletal Development*, Monograph of the Society for Research in Child Development, Washington, D. C., National Research Council, 1936, vol. 1, no. 3, pp. 1-140. (b) Todd, T. W.: *Atlas of Skeletal Maturation*, St. Louis, C. V. Mosby Company, 1937.

11. (a) Greulich, W. W.: *Some Observations on the Growth and Development of Adolescent Children*, *J. Pediat.* **19**:302-314 (Sept.) 1941. (b) Greulich, W. W.; Dorfman, R. I.; Catchpole, H. R.; Solomon, C. I., and Culotta, C. S.: *Somatic and Endocrine Studies of Pubertal and Adolescent Boys*, Monograph of the Society for Research in Child Development, Washington, D. C., National Research Council, 1942, vol. 7, no. 3 (serial no. 33), pp. 1-85. (c) Shuttleworth, F. K.: *Sexual Maturation and the Physical Growth of Girls Age Six to Nineteen*, *ibid.*, 1937, vol. 2, no. 5, pp. 1-252. (d) Shuttleworth, F. K.: *Sexual Maturation and the Skeletal Growth of Girls Age Six to Nineteen*, *ibid.*, 1938, vol. 3, no. 5, pp. 1-56.

12. Shuttleworth, F. K.: *The Physical and Mental Growth of Girls and Boys Age Six to Nineteen in Relation to Age at Maximum Growth*, Monograph of the Society for Research in Child Development, Washington, D. C., National Research Council, 1939, vol. 4, no. 3, pp. 1-291.

has been shown that in girls the rise in systolic blood pressure with age precedes menarche; after menarche there is no further systematic rise in systolic pressure during the adolescent period.¹³

Average values for girls who matured early and late as indicated by age at first menarche were calculated for each variable. Chart 5A shows the average blood pressures of 10 girls who matured early compared with the average blood pressures of 10 girls who matured later. In girls who matured early the systolic blood pressure was 2 to 8 mm. higher throughout adolescence than in girls who matured late. Chart 5B was constructed in the same manner and shows that during adolescence the pulse rate is 2 to 8 beats per minute slower in the girls who mature early than in those who mature late. Since maturity is characterized by slower pulse rate and higher blood pressure, it is apparent that girls who mature early sexually are usually advanced in maturity with respect to other physiologic variables.

Even if no other objections could be raised against using the age of menarche as a reference point to assess physiologic maturity, it is of limited value because it can be used only in girls. Since the age at which the adolescent spurt in growth reaches its maximum varies considerably

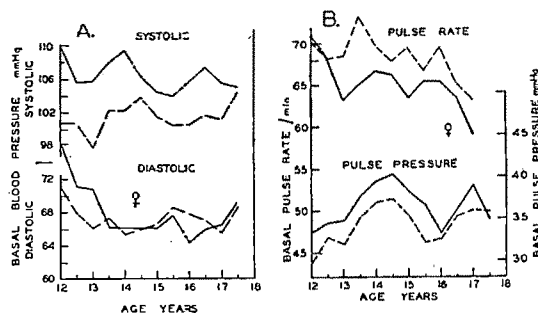


Chart 5.—Curves showing the effect of rate of maturing on basal blood pressure and pulse rate in girls. The groups were selected on the basis of age at menarche. The solid line represents the values for early maturing girls (mean age at menarche, 11.5 years); the broken line represents the values for late maturing girls (mean age at menarche, 14.75 years). Part A shows curves for the average basal systolic and diastolic blood pressures of early and late maturing groups, and part B shows similar curves for the basal pulse rates and pulse pressures.

in different persons, this characteristic may also be used as a rough index of physiologic maturity.¹² From measurements made at intervals of six months growth increments per tenth of a

13. Shock, N. W.: *The Effect of Menarche on Basal Physiological Functions in Girls*, *Am. J. Physiol.* **139**:288-292 (June) 1943.

year were calculated for a number of physical measurements of each child. Since the most uniform pattern of adolescent development was evidenced by growth in stem length, this measurement¹⁴ was used in the determination of the age of maximum rate of growth for each child, that is, in the determination of the midpoint of the period in which each child showed the maximum increment in stem length. For each sex the 10 subjects with the lowest age of maximum

highest age of maximum increment in stem length (late maturation) with respect to the cardiovascular measurements. Parts *A* and *B* of chart 6 show the curves obtained when girls are classified as having "early" or "late" maturation on the basis of the age at which they showed the adolescent spurt in growth. Parts *C* and *D* of this chart show similar data for boys. In both sexes the children who mature early have higher systolic blood pressures, higher pulse

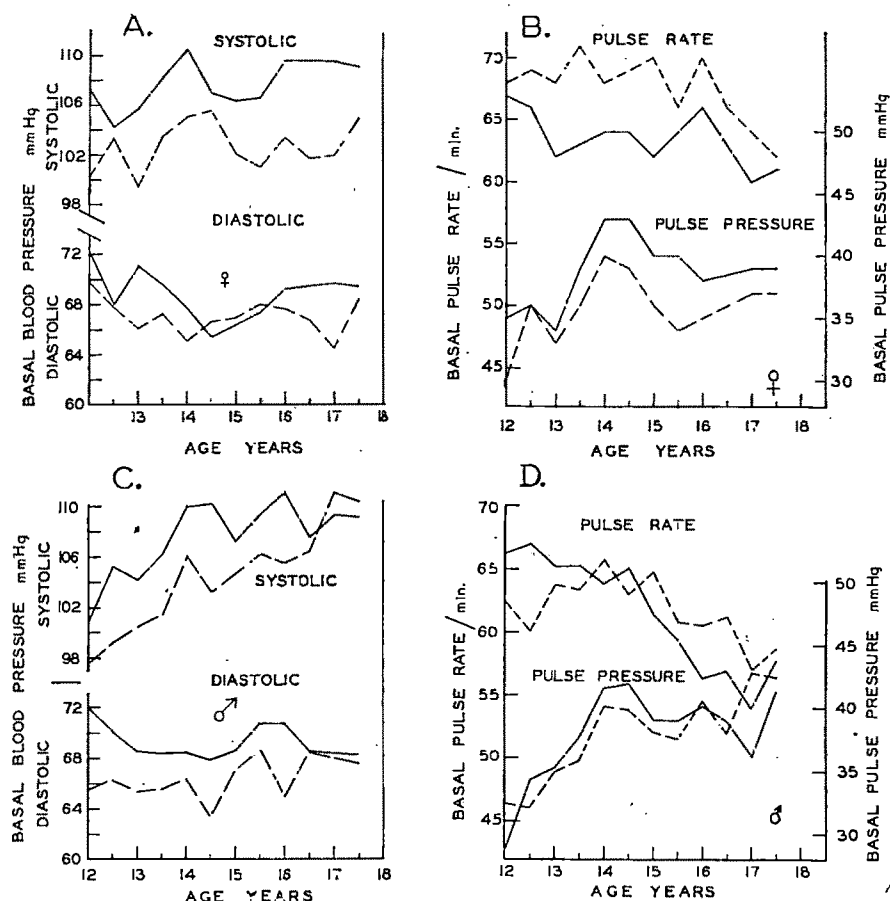


Chart 6.—Curves showing the effect of rate of maturing on basal blood pressure in girls and boys. The groups were selected on the basis of age at which maximum rate of growth in stem length occurred. *A* and *B* show the curves for girls. The solid lines represent the values for the early maturing group (mean age of maximum growth in stem length, 11.4 years); the broken lines, those for the late maturing group (mean age of maximum growth in stem length, 14.1 years). *C* and *D* show the curves for boys. The solid lines represent the values for the early maturing group (mean age of maximum growth in stem length, 13.5 years); the broken lines, those for the late maturing group (mean age of maximum growth in stem length, 15.0 years).

increment in stem length (early maturation) were compared with the 10 subjects with the

pressures and lower pulse rates throughout adolescence than children who mature later. These results offer additional evidence to support the view that in normal children the rate of growth and maturation is a general quality that finds expression in a variety of physical and physiologic areas.

COMMENT

Comparisons between the average values for pulse rate and blood pressure obtained in the

14. Stem length was measured from the top of the head to the buttocks when the child was seated with his sacral and scapular regions touching the vertical rule and with his feet resting on the seat, thus making the tuberosity of the ischium the lower limit of measurement rather than the tissue of the buttocks. This measurement is more reliable than that of sitting height. Gray, H., and Ayres, J. G.: *Growth in Private School Children*, Chicago, University of Chicago Press, 1931.)

present study and similar values reported in the literature are of limited value because of differences in the technics of estimating blood pressures and in the conditions under which the determinations were made. Furthermore, the present study differs from others reported in the literature in that the same children were measured at each age, which tends to reduce the variability of the measurements. Many discrepancies between observations of blood pressure made by different investigators may be attributed to variations in the width of the cuff used,¹⁵ the speed of compression and deflation of the cuff,¹⁶ the size of the arm in relation to the size of the cuff,¹⁷ the position of the arm and body,¹⁸ the criteria used in the estimations (palpatory or auscultatory),¹⁹ the interpretation of the sounds when the auscultatory method is used,²⁰ the degree of apprehension of the subjects,²¹ and the amount of rest permitted the subject before the measurements are made.⁶

Sutliff and Holt²² summarized the data published prior to 1925 on changes in basal pulse rate with age. These values are 8 to 10 beats per minute higher at each age than those observed in the present study. Basal pulse rates of boys reported by Robinson²³ are also higher. The lower pulse rates observed in the present study may be due in part to the greater size of the subjects at a given chronologic age, since there is a

small negative correlation between body size and pulse rate.

The average systolic pressures reported by Richey²⁴ for adolescents in Chicago are not significantly different from the values obtained in the present study; however, the average diastolic pressures reported for boys are 3 to 10 mm. lower. The diastolic pressures of girls beyond the age of 13 years reported in the two studies agree closely, but the averages reported by Richey for younger girls are 8 to 10 mm. lower than mine. Since attempts to reconcile these discrepancies must remain in the realm of conjecture, no further discussion seems warranted. The diastolic pressures observed in the present study do not differ significantly from those reported by Stocks and Karn²² for boys and by Faber and James²⁵ for children of both sexes.

The small difference between the pulse rates of boys and of girls which is apparently present even before sexual maturity may be contrasted with the definite difference between the systolic blood pressures which appears suddenly and develops rapidly after the children reach the age of 13.5 or 14.0 years. Although it has been recognized that blood pressure in normal boys and men is somewhat higher than in women and girls of the same age,²⁶ the time at which the difference first appears has not been observed previously in adolescents. To attribute the difference in blood pressure to alterations in endocrine secretion which occur with the menarche in girls is unwarranted from the present data, since other variables such as physical activity, size and metabolic rate also change at about the same time.

The statistically significant decrease in average diastolic blood pressures of children between the ages of 12 and 14.5 years has not been reported previously in the literature. Since the decrease is about 4 mm. in the average curve, it is possible that observations made on different children at each age level would fail to show any consistent decrease.

My observations indicate that during adolescence there is a significant increase in pulse pressure in both boys and girls. Although the absolute magnitudes of pulse pressures reported by Stocks and Karn²² are greater than those found by me, a similar rise of 8 to 10 mm. in pulse pressure was observed by them in British children. This rise in pulse pressure occurs at

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the time of rapid growth of the thyroid gland.²² Although neither Richey nor Faber and James observed this rise in pulse pressure during adolescence, I believe that it is characteristic of adolescent development.

SUMMARY AND CONCLUSIONS

Determinations of pulse rate and blood pressure were made for a group of 50 adolescent boys and 50 adolescent girls under basal conditions. Duplicate determinations were made for the same children on each of two successive days every six months between the ages of 11.5 and 17.5 years. Pulse rates were counted for intervals of one minute, and blood pressures were read by the auscultatory method (first and fourth sounds as the criteria for systolic and diastolic pressures respectively) by the use of a 12.5 cm. cuff and a calibrated mercury manometer. Average curves of pulse rate and blood pressure (systolic, diastolic and pulse) were prepared on the basis of chronologic age, and the pulse rates and blood pressures of early and of late maturing children were compared. Analysis of the data showed the following:

1. Under basal conditions the probable error of measurement of systolic blood pressure is 1.5 mm. of mercury for boys and 1.8 mm. for girls. For diastolic pressure the probable error of measurement is 1.8 mm. for boys and 2.2 mm. for girls. The probable error of measurement of pulse rate is 1.8 beats per minute for boys and 2.5 beats per minute for girls. These values are not significantly different from those calculated from values for adults.

2. The average pulse rate for children decreases approximately 10 beats per minute between the ages of 11.5 and 17.5 years.

3. Systolic blood pressure in boys rises significantly during adolescence (from 103 mm. Hg at 11.5 years to 115 mm. at 17.5 years), but there is no significant change in systolic blood pressure in girls over the same age span. Beyond the age of 13.5 years boys have a greater systolic blood pressure than girls of the same age.

4. The average diastolic blood pressure reaches a minimum value in persons of both sexes at the age of 14.5 years and rises continuously thereafter.

5. During adolescence the average pulse pressure for both boys and girls rises 6 to 10 mm. Hg (maximum at age 14); it returns to the pre-adolescent level by the time the person is 24 years of age. The rise is more pronounced in boys than in girls.

6. Girls who mature early with respect to menstruation and children who experience the adolescent spurt in growth early are also more mature with respect to pulse rates and blood pressures.

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The staff of the Oakland Public Schools cooperated in making the subjects available for the study. During the course of the investigation Mrs. Olga Nave, Mr. Theodor Chernikoff, Miss Helen Brien, Mrs. Katherine Heck Long, Miss Pearl Bretnall, Mrs. Mary Alice Burmeister and Mrs. Elizabeth Replogle rendered valuable technical assistance.

Baltimore City Hospitals.

EFFECTS OF REPEATED USE OF SULFADIAZINE FOR RECURRING ACUTE INFECTIONS OF THE RESPIRATORY TRACT

MORRIS SIEGEL, M.D.

NEW YORK

That sulfonamide compounds have proved themselves of great value in the therapy of various infections no longer requires experimental or clinical brief. Nevertheless, their increasing popularity among physicians in general and the introduction of new derivatives have emphasized the necessity for clarifying at least two important problems bearing on the ultimate value of these drugs. On the one hand, the question has been raised whether the repeated administration of sulfonamide drugs in successive infections in the same patient may in some way lessen their therapeutic effectiveness. On the other hand, anxiety has been expressed not only that repeated application of the different derivatives might have a cumulative injurious effect on various organs and tissues but that it might even create in time a sensitized population unable to take the drugs safely. Evidences of sensitization have been frequently reported, and the manifold manifestations ascribed to this reaction include histologic changes in various organs characterized by disseminated focal necrosis and arteritis.¹ The nature of the mechanism participating in the changes is obscure, and a definite interrelation with allergy remains to be established. For the most part the data on sensitization are based on observations on selected patients in private practice and patients under treatment at hospitals and clinics. In the absence of adequate data on the effects of repeated use of the sulfonamide drugs, the relative frequency of sensitization is at present conjectural.²

Aided by a grant from the Metropolitan Life Insurance Company.

From the Division of Infectious Diseases, the Public Health Research Institute of the City of New York.

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It seemed of value in connection with studies under way on the control of acute infections of the respiratory tract³ to determine what evidence could be furnished on the aforementioned problems, which have assumed increased importance with the widespread use of sulfonamide compounds. The clinical observations were made at Letchworth Village among feeble-minded children of recognized high susceptibility to acute infections of the respiratory tract. All of the patients under observation were treated exclusively with sulfadiazine, and none had received this drug before the present study was undertaken. It was possible, therefore, to study a large group of persons previously untreated with the drug over approximately two years and thereby determine (1) the efficacy of sulfadiazine in repeated infections, (2) the cumulative toxicity of the drug and (3) the evolution of sensitization to

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the drug. The selection of children for observation, the mental and physical characteristics of the children, their mode of living and the management of infections have all been described in earlier reports⁸ and need not be repeated.

The children studied were 149 girls living in one cottage (cottage Y) and 192 boys living in another (cottage Iota). To approximately half of the children sulfadiazine was administered at the onset of symptoms of acute respiratory disease, and the remaining half did not receive any sulfonamide compound. In addition, two other sulfadiazine-treated groups were also observed, one consisting of 23 newly admitted inmates who received 0.75 Gm. of sulfadiazine daily during the first month of residence, and the other, of 30 children who were given 1 to 2 Gm. daily for fifteen weeks.^{8d} With a daily maintenance dose of 2 Gm. the amount of free sulfadiazine per hundred cubic centimeters of blood usually varied from 4 to 10 mg.

RESULTS

Efficacy of Sulfadiazine in Repeated Infections of the Respiratory Tract.—From Oct. 1, 1941 to June 30, 1943 sulfadiazine was given one or more times to 184 children in the treatment of numerous conditions, of which acute respiratory illnesses were most common. The distribution of these children by the number of courses of treatments received follows:

Treatments * per Person	Number of Persons	Total Number of Treatments *
1.....	85	85
2.....	33	66
3.....	23	69
4.....	17	68
5.....	9	45
6.....	7	42
7 to 16.....	10	97
Total.....	184	472

* A course of therapy lasting one or more days is considered as one treatment.

Of the 184 children treated, 99 (53 per cent) received sulfadiazine on two or more occasions. The duration of the courses of therapy (also referred to as "exposures" to the drug) varied from one to one hundred and five days, with a median of four days. The total amount of sulfadiazine received during each period of therapy ranged from 1 to 148 Gm., the median being 8 Gm. The interval between treatments varied from three days to ten months, with a median of three weeks.

In studying the effects of repeated applications of sulfadiazine on the course of the acute respiratory illnesses observed, the results of the treatment of the initial infection were compared with the results of the treatment of subsequent infections of the respiratory tract. The treatment of the initial respiratory infection

during the period of observation represented the first exposure to sulfadiazine experienced by the child; the second treated infection, the second exposure to the drug, and so on. In comparing the courses of the various respiratory illnesses treated the following objective data were noted: maximum temperature on the first day of treatment, average duration of fever (rectal temperature above 100 F.), rise in temperature during the initial phases of the illness (primary rise) and subsequent rises in temperature (secondary rise). Excluded from the analysis that follows were the data for control children who became so ill as to require drug therapy and for all others who had had sulfadiazine at any time prior to their first treated respiratory illness during the period of the study. Two hundred

TABLE 1.—Comparison of Clinical Data for First and for Subsequent Infections of the Respiratory Tract in the Same Persons, Treated with Sulfadiazine

Number of Illnesses per Person	Number of Persons	Order in Which Illnesses Occurred	Average Duration of Fever, Days	Frequency of Primary Rise in Temperature		Frequency of Secondary Rise in Temperature	
				No. of Illnesses	Per Cent	No. of Illnesses	Per Cent
2	53	First	2.0	5	9.4	2	3.8
		Second	2.1	7	13.2	5	9.4
3	26	First	2.4	3	10.3	2	6.9
		Second	2.1	3	10.3	3	10.3
		Third	1.9	3	10.3	2	6.9
4	17	First	2.5	2	11.8	2	11.8
		Second	2.1	1	5.9	2	11.8
		Third	1.6	2	11.8	1	5.9
		Fourth	2.6	3	17.6	1	5.9
5	11	First	2.5	1	9.1	1	9.1
		Second	1.7	0	0.0	1	9.1
		Third	1.5	1	9.1	0	0.0
		Fourth	2.6	0	0.0	1	9.1
		Fifth	1.8	1	9.1	1	9.1

and seventy-six infections of the respiratory tract in 87 children satisfied these criteria and were therefore considered in the present study. Sulfadiazine was given for infections of the respiratory tract alone to 53 patients having 163 infections, while the remaining 34 children received the drug not only for infections of the respiratory tract but for other illnesses. All of the exposures to the drug were considered in determining the sequence of treatments.

A comparison of the data for the first and subsequent treated infections of the respiratory tract in the same children is given in table 1, in which the results obtained in the 53 children who received sulfadiazine in the treatment of infections of the respiratory tract only are summarized. Data were available for the first 2 infections in all of the 53 children, for the first 3 infections in 29, for the first 4 infections in 17 and for the first 5 infections in 11. The average duration

of fever did not vary significantly in any of these attacks. The temperature was consistently as high or higher during the first attack as during subsequent attacks. No significant differences were noted in the frequency of primary and secondary rises in temperature during the first attack and during subsequent ones.

The curves in chart 1 showing the average daily temperatures in the aforementioned infections are fairly closely superimposed, with little divergence from the mean. The differences are not considered significant. It is noteworthy that the average maximum temperature on the first day of illness was usually highest in the first infections. On the second and third days it was almost alike in all infections, and after the third day it again tended to be somewhat higher in the first infections than in the others. If the children were being sensitized or otherwise adversely affected by repeated exposures to the drug, one would expect the reverse to occur, that

instances the rise in temperature occurred during the course of drug therapy if this lasted for seven days or more; usually the temperature did not exceed 102 F. and the fever receded within forty-eight hours. The aforementioned changes in temperature were similar in character for the first and subsequent illnesses treated with

TABLE 2.—Comparison of Collective Data for the First and for Subsequent Infections of the Respiratory Tract Treated with Sulfadiazine

Infection Treated	Number of Infections	Average Duration of Fever, Days	Frequency of Primary Rise in Temperature		Frequency of Secondary Rise in Temperature	
			No. of Illnesses	Per Cent	No. of Illnesses	Per Cent
First.....	87	2.1	5	5.7	5	5.7
Second.....	63	2.1	5	7.9	6	9.5
Third.....	41	1.9	5	12.2	5	12.2
Fourth and fifth...	44	2.0	3	6.8	3	6.8
Sixth to sixteenth.	41	1.9	4	9.8	5	12.2
Total.....	276	2.0	22	8.0	24	8.7

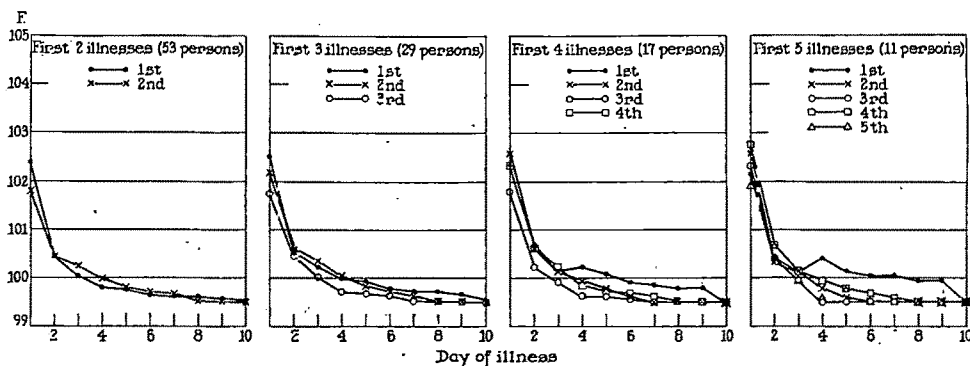


Chart 1.—Average daily temperatures in first and subsequent infections of the respiratory tract for all the persons considered in the study.

is, the maximum temperatures to be lowest in the first infections and highest in subsequent ones, particularly on the first day of treatment.

If the results for all the children considered in the study are combined, data are available on the effects of a fairly large number of primary and subsequent exposures to sulfadiazine in the treatment of infections of the respiratory tract. Summaries of these collective data are given in table 2 and chart 2. There was no significant difference in the average duration of fever in the first treated infection and in any of the others. The frequency of primary and secondary rises in temperature was somewhat lower in the first treated infection than in subsequent ones. However, the differences were not considered significant. In primary rises in temperature the maximum was usually reached on the second or third day and was usually below 102 F. Secondary rises in temperature almost always occurred between the third and the eighth day. In most

sulfadiazine. They were also observed in the the control patients, in whom they not only occurred more frequently but were more severe.³ In some treated patients the infection appeared to be sufficiently pronounced to be responsible for the rise in temperature, but the possibility of a febrile reaction to the drug in others could not be excluded.

The average daily temperatures of the treated patients during the first and subsequent infections are graphically shown in chart 2. The temperature curve showed the same trend in each group of infections; there were a sharp drop on the second day of illness and a rapid return to normal limits. The fluctuations to either side of the mean were unrelated to the sequence in which the infections occurred. In general there was no delay in recovery following repeated application of the drug. For example, the curve for the last treated infections (sixth to sixteenth), which began at a somewhat higher level than

the mean, dropped below it on the second day and remained low for the remainder of the course. These changes were indicative of prompt recoveries such as were observed in the first treated infections.

Toxic Reactions.—Treatment was interrupted in 3 children because of an obvious intolerance for the drug. Each child had extensive maculopapular dermatitis, regional lymphadenopathy and fever that receded after the drug was withdrawn. In 2 children toxic symptoms occurred during the first course of therapy, in 1 on the fifth day and in the other on the fifteenth day. The first child had no toxic effects from sulfadiazine treatment for eight subsequent infections. The other child had a recurrence of symptoms on two other occasions, on the third day of the second treated illness and on the first day of the

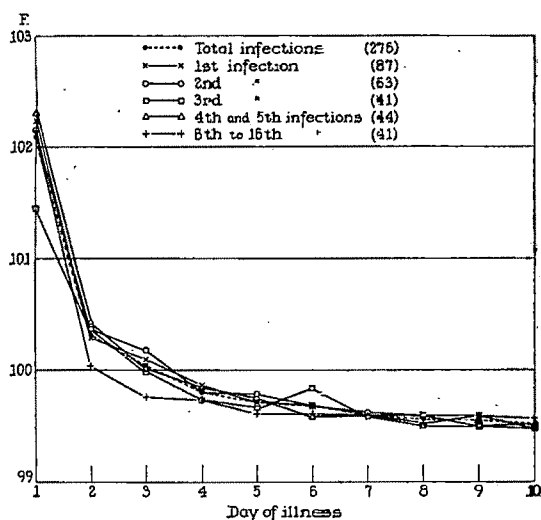


Chart 2.—Average daily temperatures in first and in subsequent infections of the respiratory tract in the same persons, treated with sulfadiazine.

third. There were no recognizable ill effects from three days' treatment of a fourth illness. The third child requiring interruption of treatment had a rash on the first day of the third treated illness. He had no discernible ill effects six weeks later during an illness that was treated for seven days.

No disturbing toxic effects were recognizable in any of the other children, even in those receiving the drug continuously for one hundred and five days.^{3d} The children who were given sulfadiazine looked as well as the controls, and they maintained their general well-being. They showed no evidences of anemia, leukopenia or obvious impairment of renal function. Their average gain in weight was comparable to the observed among the controls.

According to the foregoing data obtained at Letchworth Village, there have been no serious ill effects from the repeated or prolonged oral administration of sulfadiazine in children and the course of recurring respiratory illnesses has not been adversely affected by past exposures to this drug.

COMMENT

For almost two years sulfadiazine has been used repeatedly without serious mishap in the early treatment of acute respiratory illnesses among highly susceptible children at Letchworth Village, an institution for the feeble-minded. Repeated or prolonged application of the drug did not seem to impair the general well-being of the children treated nor their response to infections of the respiratory tract prevalent at the time. In general, the average course of the first treated infection was similar to that of subsequent treated infections.

Treatment had to be interrupted for 3 children because of extensive cutaneous eruptions which cleared after withdrawal of the drug and did not recur in 2 of the 3 children on subsequent use of sulfadiazine.

The results described emphasize the infrequency of serious ill effects following the use of sulfadiazine in children and demonstrate the safety of recurring or prolonged treatments under proper supervision. These observations supplement those of others who have stressed the relatively low toxicity of the drug.⁴

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On the other hand, there have been an increasing number of case reports on the toxicity of sulfadiazine that clearly disclose its potential dangers. In addition to the cases previously cited,^{3a, b} others have been reported. The toxic reactions reported include not only the formation of urinary concretions and renal damage⁵ but extensive pemphigoid dermatitis, severe constitutional symptoms,⁶ acute agranulocytosis,⁷ acute hemolytic anemia,⁸ acute thrombopenic purpura⁹ and the development of disseminated foci of necrosis in organs and blood vessels.¹⁰ While

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some of the toxic effects ascribed to sulfadiazine may be coincidental changes etiologically unrelated to the drug,¹¹ others are undoubtedly caused by it. Even though the toxic effects of clinical importance are generally readily recognizable and usually recede after prompt withdrawal of the drug, the occasional deaths attributable to sulfadiazine¹² present a serious threat that confronts the practitioner. Although indiscriminate application of the drug is admittedly unjustifiable, the excessive delay in treatment occasioned by timidity is also unwarranted and contributes to considerable suffering and an unknown number of deaths. Both extremes of attitude are reprehensible and accentuate the need for greater knowledge of the effects of the drug and wider dissemination of available information.

SUMMARY

In a study of the effects of repeated oral administration of sulfadiazine in the treatment of children with recurring acute infections of the respiratory tract from October 1941 through June 1943 the courses of the first and of the subsequent infections appeared to be comparable within the normal limits of sampling variability. The recognizable toxic effects of sulfadiazine were infrequent and were controlled by prompt withdrawal of the drug.

According to the experience described, the frequency of sensitization to sulfadiazine and of cumulative damage to organs and tissues must be considered of a low order.

Dr. Harry C. Storrs, Superintendent of Letchworth Village, aided in this work.

The sulfadiazine was supplied by Lederle Laboratories, Inc., Pearl River, N. Y.

Foot of East Fifteenth Street.

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Case Reports

FETAL ERYTHROBLASTOSIS AND HABITUAL ABORTION

THEODORE D. COHN, M.D., AND SEYMOUR L. COLE, M.D.

BEVERLY HILLS, CALIF.

The concept of erythroblastosis fetalis as a hemolytic familial disease entity has become firmly established. Ottenberg¹ was the first to suggest an antigen-antibody relationship between the red blood cells of the fetus and the blood of the mother. Macklin² observed that mothers of infants with erythroblastosis fetalis were subject to spontaneous abortions, miscarriages and stillbirths. Landsteiner and Wiener³ demonstrated the Rh factor, an agglutino-gen transmitted as a simple mendelian dominant characteristic and found in the red blood cells of 85 per cent of human beings. An erythroblastotic fetus inherits from the father the agglutino-gen which determines the Rh positivity of the blood. Levine, Katzin and Burnham⁴ and Levine, Burnham, Katzin, and Vogel⁵ demonstrated the association of erythroblastosis fetalis with the Rh factor on the basis of isoimmunization. The modern concept is actually an application of the principles of isoimmunization laid down by Ehrlich and Morgenroth in 1900.⁶ Rh agglutino-gen from an infant with Rh-positive blood passes through the imperfect placental barrier into the blood of the mother. If the blood of the mother is Rh negative, anti-Rh agglutinins are produced in response to the Rh agglutino-gen. They then pass through the placenta into the fetal blood, where they cause hemolysis of the fetal Rh-positive cells and produce the manifestations of fetal erythroblastosis.

REPORT OF A CASE

The patient, a 34 year old white woman, was married for the first time in 1931, at the age of 23.

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2. Macklin, M. T.: Erythroblastosis Foetalis, *Am. J. Dis. Child.* **53**:1245 (May) 1937.

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4. Levine, P.; Katzin, E. M., and Burnham, L.: Isoimmunization in Pregnancy, *J. A. M. A.* **116**:825 (March 1) 1941.

5. Levine, P.; Burnham, L.; Katzin, E. M., and Vogel, P.: The Role of Isoimmunization in the Pathogenesis of Erythroblastosis Foetalis, *Am. J. Obst. & Gynec.* **42**:925 (Dec.) 1941.

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Between 1931 and 1934, she had two spontaneous abortions, one at two months, the other at three months.

In 1935 she became pregnant again and delivered an eight month, premature, severely jaundiced infant. A diagnosis of erythroblastosis fetalis was made; the child died in two days. An autopsy revealed a six week premature infant girl with jaundiced scleras and skin and a distended abdomen. There were small amounts of clear jaundiced fluid in the pleural, pericardial and peritoneal cavities. Microscopically, areas of hemo-poietic tissue were found in the liver, pancreas, adrenal glands and lymph nodes. The sternal and tibial marrow was shown to be hyperplastic, with an increase in the erythroid elements. The blood showed severe erythroblastosis.

The patient was divorced in 1936. In 1938 she re-married. During the interval from 1938 to 1940 she had three pregnancies, in 1938, 1939 and 1940, all of which terminated in spontaneous abortions in the second and third month.

Still hoping for a viable child, the patient became pregnant once more in 1941. In view of the history of repeated abortions and the premature delivery of an erythroblastotic infant, tests for the Rh factor were performed on the blood of the patient and of her second husband.

The patient's blood was found to be Rh negative; her husband's, Rh positive. While these studies were in progress, the patient took a long train trip, shortly after which she spontaneously aborted a two month fetus.

At this time the patient's first husband was traced, and a sample of his blood was obtained for study. It proved to be Rh positive. In the interim he had re-married, and his second marriage was productive of a normal child.

The patient became pregnant again in 1942 but once more could not carry through. She spontaneously miscarried twins at six months' gestation.

COMMENT

According to Diamond, Blackfan and Baty⁷ erythroblastosis fetalis is manifested clinically by one of three predominant symptom complexes: icterus gravis neonatorum, universal edema of the newborn and congenital anemia of the newborn. The condition of the infant born to this patient in 1935 conformed classically to the icterus gravis neonatorum form of the disease.

The identification of the antigen-antibody combination evolved through the correlation of studies

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of the reactions to intragroup transfusions in obstetric cases with studies of the blood of erythroblastotic infants and of their parents. In these studies it was shown that fetal erythroblastosis was due to an agglutininogen-agglutinin reaction and that the end result was hemolysis in the fetal blood. Isoimmunization explains the blood picture and the familial incidence of the disease.

The proportion of anti-Rh agglutinins in the mother's blood was found to diminish with the lapse of time after pregnancy, although in a few instances the agglutinins were present two months to a year or more post partum.

To quote Levine, Burnham, Katzin and Vogel,⁵ "Since antibody production in general is characterized by a gradual rise, a period of maximum activity and gradual disappearance, it is conceivable that in some cases anti-Rh agglutinins, after exerting their lytic effect on the fetus, rapidly disappeared from the blood so that none could be demonstrated at the time of delivery."

From the above observation it is suggested that immune isoagglutinins reaching a peak of action early in the course of pregnancy produce either abortions or miscarriages. Those acting later may be responsible for erythroblastosis fetalis. Isoimmunization occurring near term may be responsible for relatively mild congenital anemia of the newborn infant. These factors might well have occurred in this patient as demonstrated by spontaneous abortions in the second and third months, miscarriage of twins in the sixth month and premature delivery of an eight month fetus with erythroblastosis fetalis.

Factors serving to limit the incidence of erythroblastosis fetalis may include individual resistance to any type of active immunization, impenetrability of the placental barrier, variation in the potencies and titers of the Rh factor and of the agglutinins thus produced and processes tending to inactivate the Rh factor in the maternal blood or the anti-Rh agglutinin in the fetal blood.

In the treatment of erythroblastosis fetalis transfusions play an important part. Only persons with Rh-negative blood should be used as donors, so that the cells may not be hemolyzed by any anti-Rh agglutinins remaining in the recipient's blood.

Mothers of erythroblastotic infants should not be permitted to nurse their children, since anti-

Rh agglutinins may be transmitted in the mammary secretions.⁸

If artificial insemination is contemplated for the sake of viable children in mothers who have been denied them because of isoimmunization, it is necessary that the prospective sperm donor have Rh-negative blood. Cross matching between the blood of the donor and that of the recipient should be performed.

To carry the theoretic procedure a step further, if premarital tests for the Rh factor were practical, the occurrence of erythroblastosis fetalis could be foreseen and prevented. Certainly, however, every case of habitual abortion should be studied for the presence or absence of the Rh factor.

SUMMARY

Habitual abortion and production of an infant with erythroblastosis fetalis occurred in a mother whose blood was Rh negative with two successive husbands, both of whom had Rh positive blood.

According to the present concept of the causation of the disease the fetus inherits the Rh factor from a father with Rh-positive blood. The Rh factor (agglutininogen) passes through an imperfect placental barrier into the Rh-negative blood of the mother. In response to the Rh agglutininogen, anti-Rh agglutinins are produced. These agglutinins pass through the placenta into the fetal blood, where they cause hemolysis of fetal red blood cells and produce the manifestations of erythroblastosis fetalis.

It is suggested that only Rh-negative blood should be used in the treatment of the disease and that mothers of erythroblastotic infants should not be permitted to nurse their children.

It is important to obtain a person with Rh-negative blood as a sperm donor if artificial insemination is contemplated for the mother of an erythroblastotic infant.

If premarital cross matching and tests for the Rh factor were performed the occurrence of erythroblastosis fetalis could be foreseen and prevented.

In all cases of habitual abortion tests for the Rh factor and its agglutinin should be made.

123 North San Vincente Boulevard.

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FULMINANT MENINGOCOCCEMIA TREATED WITH PENICILLIN CALCIUM

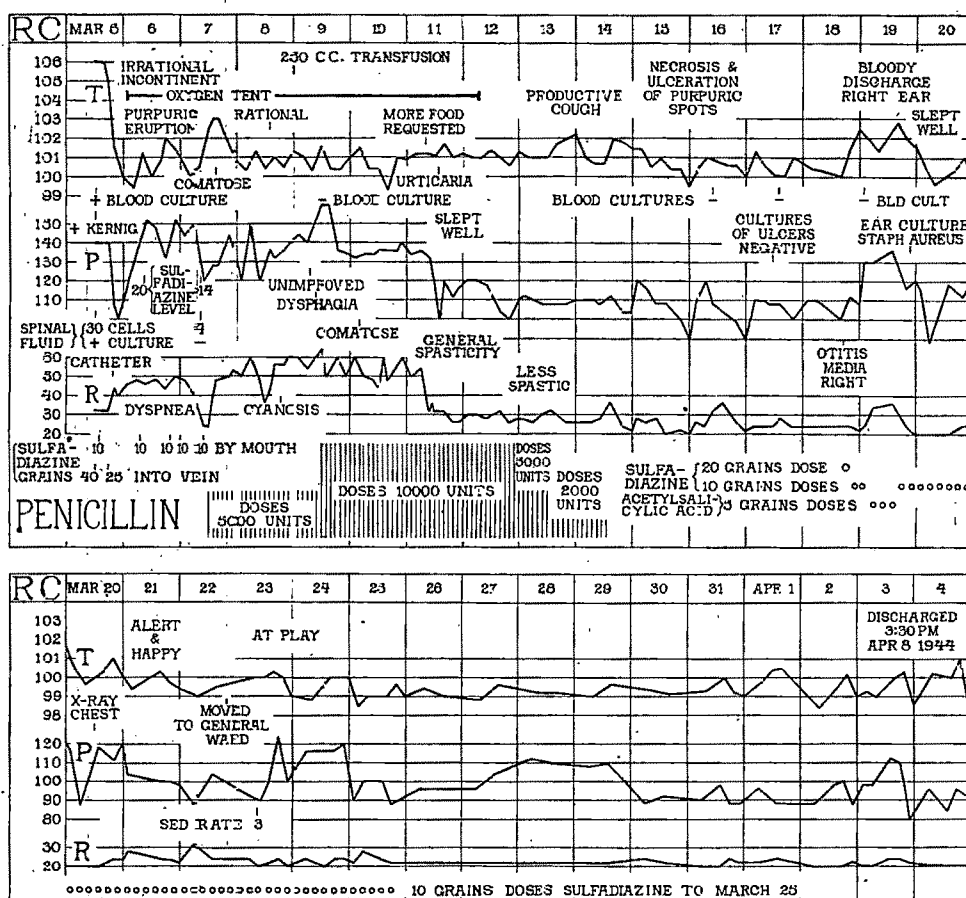
WARD J. MACNEAL, M.D., AND MARSHALL C. PEASE, M.D.

NEW YORK

Martland¹ recently reported 19 fatal cases of the Waterhouse-Friderichsen syndrome, characterized by cyanosis, purpura, petechiae and bilateral gross hemorrhages in the adrenal glands, and by the presence of meningococci in the blood, without gross meningitis. Attempts to overcome the profound meningococcemia in 5

the disease. Martland suggests that the usefulness of penicillin in the treatment of patients with fulminant meningococcemia is still a matter of conjecture.

We wish to report briefly regarding a boy of 8 years admitted to the hospital seemingly near death, with overwhelming meningococcemia, who



Abbreviated clinical record of R. C.

of the patients by intravenous injections of solutions of sulfadiazine and dextrose were futile and made no apparent impression on the course of

was treated with sulfadiazine intravenously and by mouth for two days without result and then with penicillin intravenously and intramuscularly with complete success.

From the Department of Bacteriology and the Department of Pediatrics, New York Post-Graduate Medical School and Hospital, Columbia University.

1. Martland, H. S.: Fulminating Meningococcal Infection with Bilateral Massive Adrenal Hemorrhage (the Waterhouse-Friderichsen Syndrome), Arch. Path. 37:147-158 (Feb.) 1944.

REPORT OF A CASE

R. C., a white boy born Sept. 10, 1935, was admitted to the New York Post-Graduate Hospital on March 5, 1944. At birth he had weighed 5 pounds, 6 ounces (2,438 Gm.). He was not breast fed. His food had included vitamins. He had had whooping cough in 1936,

measles in 1938 and frequent colds, and a tonsillectomy was performed in 1938. Both parents were living and well. One brother, aged 15 years, had been mentally defective since birth.

On Feb. 26, 1944, the patient complained of dizziness and headache which persisted for two days. About March 3 a slight cold with running nose developed, and it persisted. However, on March 4 the patient engaged in his usual activities. On the evening of March 4 his temperature rose suddenly to 104 F. and he complained of pains in his legs and in the back of his head. Soon thereafter there were chills, projectile vomiting and delirium; ten hours after the observation of fever he was seen by a physician, who advised immediate hospitalization. He was carried into the hospital at 12 noon, March 5, 1944. At this time he was pale, cyanotic, irrational, with imperceptible pulse and with numerous petechiae over the body and extremities but not on the face. Respiration was shallow, with occasional dyspnea. A slight purulent nasal discharge was noted. The heart sounds were hardly audible, and the rate was extremely rapid, but no murmurs could be distinguished. The Babinski sign was positive on the right side and the Kernig and Brudzinski signs were positive on both sides. The diagnosis at the patient's admission was (1) meningococcic septicemia and (2) possible meningococcic meningitis.

Spinal fluid removed at about 12:10 p. m. contained a small amount of blood, and the few colonies of bacteria which appeared on culture plates inoculated with the spinal fluid may have come from the blood. A specimen of blood taken at the same time yielded an enormous number of colonies of meningococci in pure culture, many hundreds per millimeter of the patient's blood. At 12:10 p. m. intravenous infusion of 600 cc. of 2.5 per cent dextrose solution containing 40 grains (2.3 Gm.) of sulfadiazine sodium was started. The subsequent doses are indicated on the graphic chart. The patient was kept in an oxygen tent almost continuously. His condition remained desperate. On the morning of March 7 he became violently delirious and climbed over the side of his bed, but no apparent injury resulted. He was incontinent, restless and noisy and struggled and chewed at his restraining bandages. However, he did swallow fluids in small quantities.

At 11:57 a. m. on March 7 the first dose of penicillin was given intravenously, 5,000 units of the sodium salt in 5 cc. of isotonic solution of sodium chloride, and this amount was given again at 1:57 p. m. Soon thereafter a supply of the calcium salt² arrived, and this was used exclusively for the subsequent penicillin therapy indicated in the chart. On March 8 there was no evidence of improvement, and on March 9 there was progressive deterioration, increasing weakness, dyspnea, cyanosis and edema of the ankles. Endocarditis was considered certain, but even with acceptance of this diagnosis the lack of favorable response was disappointing. Respiration continued to be rapid even in the oxygen tent. Blood obtained at noon on March 9 remained culturally sterile. At that time the dose of penicillin was increased to 10,000 units every two hours.

2. The penicillin calcium was supplied by Chas. Pfizer & Company, 11 Bartlett Street, Brooklyn, in response to an urgent emergency appeal.

On March 11 there was dramatic improvement but with persistence of general spasticity. The pulse and respiration became much better, and oxygen therapy was discontinued on the morning of March 12. The dose of penicillin was reduced to 5,000 units the following midnight and to 2,000 units after the noon dose on March 13, and the administration was discontinued altogether the next afternoon (March 14). During the days of rapid improvement there was a productive cough; evidently there had been rather severe septic pneumonitis, which was now resolving.

Many of the purpuric spots on the skin became necrotic and sloughed, producing small deep ulcers. Material from several of the ulcers was cultured, but no organisms were demonstrated, suggesting that the meningococci originally concerned in their causation had been exterminated. All cultures of the blood, except the initial one of March 5, also remained sterile. Definite meningitis did not develop. However, there was inflammation of the right ear on March 18, with a bloody purulent discharge on the next day that yielded *Staphylococcus aureus* on culture. The patient was removed from isolation on March 22 and discharged in good condition on April 8.

The calcium salt of penicillin was given either intravenously or by intramuscular injection every two hours in doses of 5,000 units for two days and then in doses of 10,000 units every two hours for three and a half days more. There was mild urticaria on March 11, the fifth day of penicillin therapy, coincident with rapid general improvement of the patient's condition. We did not observe any other untoward effect which could be ascribed to the penicillin.

It is, of course, impossible to maintain that this boy would have died without penicillin. He was apparently moribund on admission, and the sulfadiazine seemed to prevent the impending death, though it appeared that death was merely being postponed by this agent. After the penicillin therapy was started, the issue of life and death remained in the balance for three days. Past experience with malignant fulminant meningococcemia has not inspired confidence in any therapy for this condition, and in the present instance the situation seemed hopeless from March 5 to March 10. The calcium salt of penicillin was evidently harmless, even in doses of 120,000 units per day, to a boy of 8 years, weighing about 60 pounds (about 27 Kg.).

SUMMARY

A boy of 8 years recovered from fulminant meningococcemia after treatment first with sulfadiazine and subsequently with penicillin. The calcium salt of penicillin was found satisfactory and produced no serious untoward effects.

303 East Twentieth Street.

155 East Sixty-Second Street.

Progress in Pediatrics

PRESENT STATUS OF THE RH FACTOR

EDITH L. POTTER, M.D., PH.D.

CHICAGO

The manner in which laboratory experiments were correlated with clinical data and the importance of the Rh factor in relation to the causation of erythroblastosis and of certain reactions to intragroup transfusions was established as one of the most interesting stories in recent medical literature. The short time that has elapsed since the Rh factor was first described has been sufficient to permit numerous investigations, and over one hundred papers on various phases of this subject have already been published. In common with many new discoveries its importance may be currently overemphasized, and the ultimate place the Rh factor will take in medical thought and practice cannot yet be foretold. There are numerous problems still to be solved, but in the following pages an attempt will be made to summarize the available information that exists at present.

HISTORICAL BACKGROUND

Incompatible Blood as a Cause of Fetal and Maternal Morbidity.—Some form of incompatibility between the mother and the fetus as a cause of morbid conditions in one or the other has been considered intermittently for many years. Dienst,¹ in 1905, was the first to note that when the mother's blood contained an α or β agglutinin incompatible with the fetal cells the agglutinin titer of her serum was frequently higher four to eight days after delivery than it had been previously. He believed that the rise in titer resulted from the antigenic action of fetal cells that had gained entrance to the maternal circulation and that this increase in antibody titer was a cause of eclampsia. Murray (1910)² considered hemagglutinins and hemolysins from the fetus as a cause of maternal toxemia but dismissed the idea as improbable after learning that fetal isoagglutinins were frequently nonexistent at birth.

Somewhat later McQuarrie³ found that the fetus and the mother were of incompatible blood groups in 70 per cent of 180 cases of toxemia. He thought that the normal placenta was inviolable, but he believed that occasionally a break occurred and fetal cells gained access to the maternal circulation. The thrombi present in some of the necrotic areas characteristic of livers of women with fatal eclampsia of pregnancy were believed to be clumps of fetal cells.

Gruhzit⁴ in 1923 stated that while incompatibility between maternal and fetal blood existed in only 3 of 86 normal pregnancies it was uniformly present in 16 cases of eclampsia or pre-eclampsia. He concluded that a specific agglutinable substance from the fetal erythrocytes passes to the mother's system as a fetal waste product and in the mother's blood stream is agglutinated and suspended in fine colloidal particles; the presence of a colloidal substance produces an increase in the viscosity of the blood, which in turn causes the symptoms of toxemia. Gruhzit also suggested⁵ that incompatibility of blood groups might be responsible in some cases for idiopathic sterility and miscarriage.

About the same time Ottenberg⁶ discussed the findings of Dienst and McQuarrie and concurred in the belief that eclampsia was most often due to immunization of the mother by the continuous introduction of small numbers of incompatible fetal cells into her blood. In the last paragraph of his paper he suggested that jaundice of the newborn and certain types of hemorrhagic disease might be due to accidental placental transfusion of incompatible blood. This seems to mean that he believed maternal cells could enter the fetal circulation and reverse the process thought to initiate eclampsia.

That the agglutinin titer of maternal serum rises during pregnancy if the fetal blood is of a group incompatible with that of the mother and that the incidence of incompatibility is greater

From the Department of Obstetrics and Gynecology, University of Chicago, and Chicago Lying-in Hospital.

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2. Murray, H. L.: The Haemotoxic Nature of Eclampsia, with an Account of the Foetal and Placental Hemolysins and an Experimental Investigation into the Anaphylactic Theory of Eclampsia, J. Obst. & Gynaec. Brit. Emp. 18:225, 1910.

3. McQuarrie, I.: Isoagglutination in Newborn Infants and Their Mothers, Bull. Johns Hopkins Hosp. 34:51, 1923.

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in toxemic than in nontoxemic patients was denied by Allen ⁷ in 1926 after studying 104 toxic and 375 nontoxic patients. He found that in approximately 21 per cent of both groups of patients the mothers and infants were of incompatible blood groups and that the average agglutinin titer was 1:79 for toxic as well as for nontoxic patients.

The possibility that differences in blood groups might be responsible for erythroblastosis was mentioned by Hirsfeld ⁸ in 1928 and Paroli ⁹ in the same year reported that among 27 women who had had abortions only 1 was of the same blood group as her husband. Jonsson ¹⁰ in 1936 again confirmed the statement that the titer of anti-A or anti-B agglutinins in maternal serum rises appreciably when the cells of the fetus are incompatible with those of the mother.

In 1938 Darrow ¹¹ reviewed the literature on erythroblastosis and from an analysis of the published data concluded that the best explanation for erythroblastosis lay in an antigen-antibody reaction. She made no mention of differences in the AB antigens present in the blood of the mother and of the fetus as a cause of the antigenic reaction but postulated a difference in the chemical components of fetal and of adult hemoglobin which would make possible a maternal sensitization to the fetal type. Darrow thought that the disease could be produced in the fetus by the transmission of maternal antibodies through the placenta and in the infant after birth by the ingestion of antibodies in breast milk. Her reasoning was logical, and her theory of the causation of erythroblastosis explained many of the conditions associated with this disease. Some support for this theory was subsequently obtained when she and her collaborators ¹² produced antisera in rabbits that differentiated fetal from adult hemoglobin.

Reactions to Intragroup Transfusions.—Prior to the establishment by Landsteiner ¹³ in 1900

of the group-specific character of human erythrocytes, intravenous administration of blood had not been practicable because of the severe reactions that followed its introduction into the circulation. After the four major groups were discovered ¹⁴ and a simple method for their determination was established, ¹⁵ it was possible to give transfusions with relative impunity. Continued investigation revealed the presence of subdivisions in groups A and AB in 1911 ¹⁶ and in 1927 ¹⁷ additionally recognized individual properties of human blood were designated M, N and P. Other irregular agglutinins have been demonstrated, ¹⁸ the majority of which were more active at 0 C. than at 20 C. or 37 C. These are known as cold agglutinins because of their greater activity at low temperatures, and they often agglutinate the person's own cells as well as those of others in the same blood group. They appear to be of practically no significance as far as reactions to transfusions are concerned.

Landsteiner and Levine in 1929 ¹⁹ and 1930, ²⁰ while studying blood from 500 patients, found a high percentage of cold agglutinins and observed that the action of 3 per cent of these agglutinins persisted at room temperature. Five of the patients received transfusions of blood the cells of which were agglutinated at 20 C. by the recipient's serum. No reactions followed. This observation is of special interest in relation to the present belief that blood showing such agglutination should never be administered.

A few hemolytic reactions were known to occur, however, that could not be explained by the presence of any known agglutinin. In reviewing the literature available by 1940 it is evident that these reactions occurred largely in pregnant or previously pregnant women ²¹ or in persons who had previously been given transfusions. ²² Wiener

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18. Landsteiner, K., and Levine, P.: On the Cold Agglutinins in Human Serum, *J. Immunol.* **12**:441, 1926.

19. Landsteiner, K., and Levine, P.: On Isoagglut-inins Reactions of Human Blood Other Than Those Defining the Blood Groups, *J. Immunol.* **17**:1, 1929.

20. Landsteiner, K., and Levine, P.: On the Inher- itance and Racial Distribution of Agglutinable Prop- erties of Human Blood, *J. Immunol.* **18**:87, 1930.

and Peters²³ called attention to this fact at that time.

Stetson^{21a} in 1933 reported the extremely interesting history of a young woman who had had 5 normal children. After an induced abortion at two months she had been given five transfusions. The first, from a brother, was uneventful; the second, from a professional donor, was also uneventful, but the donor's cells were later shown to be agglutinated by the patient's serum. The third transfusion was from the husband and was followed by a severe reaction; the fourth and fifth transfusions, from 2 of the patient's brothers, were also uneventful. This case caused much speculation on the part of the author as to why the early transfusions were satisfactory, why the cells of members of the family were all compatible and why the husband's blood

should have caused such a severe reaction. He concluded that an inherited latent isoagglutinin might be present in several members of the family and that introduction of foreign blood might stimulate the development of agglutinin to a point where the titer would be sufficiently high to cause agglutination of all cells from persons outside of the family. The author wished to attempt to induce the formation of the antibody in one of the patient's brothers but was refused. Had the brother cooperated, successful immunization might well have been accomplished. In view of our present knowledge the reaction exhibited by this patient seems to have been a definite example of immunization to the Rh factor.

Culbertson and Ratcliffe^{21b} in 1936 described 2 patients whose serum agglutinated the cells of many members of the same blood group. They commented on the fact that the mother of 1 patient was the only person whose cells the patient's serum did not agglutinate. They also noted that both patients had recently been pregnant and stated: "Although we attach no significance to the fact, it should be noted that in both cases the intragroup agglutinin was demonstrated during the puerperium."

Parr and Krischner^{21c} and Goldring and Graef^{21d} each reported reactions to transfusions of husband's blood to a patient with hemorrhage following an abortion. Both patients recovered.

However, not until 1939, when Levine and Stetson^{22a} reported "an unusual case of intragroup agglutination," was the suggestion made that pregnancy might be specifically related to the presence of atypical intragroup agglutinins. These authors observed a woman whose serum agglutinated the cells of 80 per cent of all persons in the same blood group and suggested that she might have become immunized to some agent that the fetus had inherited from the father. The fetus had been harbored in a nonliving state for six weeks before it was delivered.

The stage was thus set for the developments which were to follow in rapid succession. It had been shown that when atypical agglutinins capable of causing a reaction at transfusion were present (1) the patient had either previously had transfusions or recently been pregnant, (2) if the patient had recently been pregnant the pregnancy had often terminated with abortion or intrauterine death of the fetus, (3) blood cells of the patient's siblings or parents were often the only ones not agglutinated by the patient's serum and (4) transfusion of the husband's blood was frequently responsible for a reaction. The suggestion had been made that the fetus, because of its inheritance from the father of an antigen

21. (a) Stetson, R. E.: Causes and Prevention of Posttransfusion Reactions, *S. Clin. North America* **13**: 319, 1933. (b) Culbertson, C. G., and Ratcliffe, A. W.: Reaction Following Intra-Group Blood Transfusion: Irregular Agglutinin Demonstrated by the Sensitive Centrifuge Test Method, *Am. J. M. Sc.* **192**:471, 1936. (c) Parr, L. W., and Krischner, H.: Hemolytic Transfusion Fatality with Donor and Recipient in Same Blood Group, *J. A. M. A.* **98**:47 (Jan. 2) 1932. (d) Goldring, W., and Graef, I.: Nephrosis with Uremia Following Transfusion with Incompatible Blood, *Arch. Int. Med.* **58**:825 (Nov.) 1936. (e) Johnson, R. A., and Conway, J. F.: Urinary Suppression and Uremia Following Transfusion of Blood, *Am. J. Obst. & Gynec.* **26**:255, 1933. (f) Von Deesten, H. T., and Cosgrove, S. A.: Renal Insufficiency Following Blood Transfusion: Recovery After Venesection, *Ann. Int. Med.* **7**:195, 1933. (g) Smith, C. E., and Haman, J. O.: Reaction Following Blood Transfusion, *California & West. Med.* **41**: 157, 1934. (h) Zacho, A.: "Unverträglichkeit" zwischen Blutproben vom gleichen Bluttypus, beruhend auf dem Vorhandensein eines irregulären Agglutinins gegenüber einem bisher unbekannten Rezeptor, *Ztschr. f. Rassenphysiol.* **8**:1, 1936. (i) Pondman, A.: Difficulties in Blood Group Determination, *Nederl. tijdschr. v. geneesk.* **82**:6111, 1938; cited by Wiener and Peters.²³ (j) Mandelbaum, H. M.: Hemolytic Reactions Following Blood Transfusion: Report of a Case of Intra-Group Incompatibility, *Ann. Int. Med.* **12**:1699, 1939. (k) Bernstein, A.: Anuria Following Blood Transfusion, *Am. J. Obst. & Gynec.* **39**:1045, 1940. (l) Hamilton, E. G., and Martini, A. P.: Blood Transfusion in Pregnancy: A Review of Three Thousand Cases, *ibid.* **43**:313, 1942.

22. (a) Neter, E.: Observations on Abnormal Antibodies Following Transfusions, *J. Immunol.* **30**:255, 1936. (b) DeGowin, E. L., and Baldrige, C. W.: Fatal Anuria Following Blood Transfusions: Inadequacy of Present Tests for Compatibility, *Am. J. M. Sc.* **188**:555, 1934. (c) Baron, C.: The Present Status of Hemolysis in Blood Transfusions with Report of a Fatal Case, *Kentucky M. J.* **30**:326, 1932. (d) Levine, P., and Stetson, R.: Unusual Case of Intra-Group Agglutination, *J. A. M. A.* **113**:126 (July 8) 1939.

23. Wiener, A. S., and Peters, H. R.: Hemolytic Reactions Following Transfusions of Blood of the Homologous Group with Three Cases in Which the Same Agglutininogen Was Responsible, *Ann. Int. Med.* **3**:206, 1940.

lacking in the mother, might be the source of the factor producing an immune state in the mother.

Discovery of the Rh Factor and Establishment of its Clinical Significance.—It had been known for some time that certain substances and the blood of certain animals when injected into test animals produced antibodies capable of reacting with blood cells other than those inciting their production. In 1937 Landsteiner and Wiener²⁴ produced anti-M agglutinins in rabbits by the injection of blood from the rhesus monkey *Macaca mulatta*. Following this line of investigation they²⁵ later obtained an antirhesus serum which after absorption to remove antibodies characteristic of the species still contained an agglutinin (unrelated to any previously described) that agglutinated the cells of 39 of 45 human bloods. The agglutinin thus identified was designated Rh because of its presence in the cells of the rhesus monkey. Human cells that were agglutinated by the antirhesus (anti-Rh) serum were designated as Rh positive (Rh +), and those not agglutinated, as Rh negative (Rh —).

Shortly thereafter Wiener and Peters²³ observed 3 patients who had had severe reactions after receiving transfusions of homologous blood. The action of antibodies found in the blood of these patients paralleled that of the anti-Rh agglutinins. It was concluded that in these patients the production of antibodies had been stimulated by the previous administration of Rh-positive blood and that the subsequent introduction of similar cells resulted in agglutination and hemolysis.

Later in 1940 Levine and his co-workers²⁶ observed that the serums of several patients who had had repeated miscarriages or abortions contained atypical isoagglutinins related to the Rh factor, and in 1941 Katzin found that the serum of the patient previously described by Levine and Stetson^{22d} agglutinated the same cells as the newly discovered anti-Rh rabbit serum. Had it been possible to retest the patients previously described by Zacho, Neter, Stetson, Culbertson and Ratcliffe and others, they also could prob-

ably have been shown to possess an agglutinin identical with or related to the antirhesus agglutinin. Additional papers published within a short time by Levine and Polayes,²⁷ Wiener²⁸ and Scott and Conant²⁹ gave further support to the belief that Rh-positive blood introduced by transfusion or from the placenta could produce immunization.

Soon after the realization that a specific antibody was present in certain patients who had had a high incidence of unsuccessful pregnancies, Levine, Katzin and Burnham³⁰ thought it significant that a diagnosis of erythroblastosis had been made on some of the dead fetuses. In further investigations on the blood of other women who had had infants with this disease they and Vogel³¹ found that the majority of the mothers had Rh-negative blood, in contrast to the high percentage of women in the general population whose blood was Rh-positive. In a paper by Burnham³² and in two editorials by Levine³³ that appeared during 1941 further attention was called to the relationship of the Rh factor to erythroblastosis, and the theory of an immunologic basis for erythroblastosis became fairly well established. It was shown that erythroblastosis and possibly other conditions affecting the fetus or the newly born infant were the result of an antigen-antibody reaction: Rh-positive fetal cells entering the maternal blood were believed to stimulate the formation of anti-Rh agglutinins; maternal agglutinins passing

27. Levine, P., and Polayes, S. H.: An Atypical Hemolysin in Pregnancy, *Ann. Int. Med.* **14**:1903, 1941.

28. Wiener, A. S.: Hemolytic Reactions Following Transfusions of Blood of Homologous Group: Further Observations on the Role of Property Rh, Particularly in Cases Without Demonstrable Isoantibodies, *Arch. Path.* **32**:227 (Aug.) 1941.

29. Scott, J. E., and Conant, J. S.: Successful Transfusions Following Previous Hemolytic Transfusion Reaction Due to Rh and Anti-Rh Factors: Report of Case, *Am. J. Clin. Path.* **11**:536, 1941.

30. Levine, P.; Katzin, E. M., and Burnham, L.: Isoimmunization in Pregnancy: Its Possible Bearing on the Etiology of Erythroblastosis Foetalis, *J. A. M. A.* **116**:825 (March 1) 1941.

31. (a) Levine, P.; Vogel, P.; Katzin, E., and Burnham, L.: Pathogenesis of Erythroblastosis Foetalis: Statistical Evidence, *Science* **94**:371, 1941. (b) Levine, P.; Burnham, L.; Katzin, E., and Vogel, P.: The Role of Iso-Immune in the Pathogenesis of Erythroblastosis Foetalis, *Am. J. Obst. & Gynec.* **42**:925, 1941.

32. Burnham, L.: Common Etiology of Erythroblastosis and Transfusion Accidents in Pregnancy, *Am. J. Obst. & Gynec.* **42**:389, 1941.

33. (a) Levine, P.: The Role of Iso-Immune in Transfusion Accidents in Pregnancy and in Erythroblastosis Foetalis, *Am. J. Obst. & Gynec.* **42**:165, 1941.

(b) Levine, P.: The Role of Iso-Immune in Transfusion Accidents and in the Pathogenesis of Erythroblastosis Foetalis, *Am. J. Clin. Path.* **11**:898, 1941.

24. Landsteiner, K., and Wiener, A. S.: On the Presence of M Agglutinogens in the Blood of Monkeys, *J. Immunol.* **33**:19, 1937.

25. Landsteiner, K., and Wiener, A. S.: An Agglutinable Factor in Human Blood Recognized by Immune Sera for Rhesus Blood, *Proc. Soc. Exper. Biol. & Med.* **43**:223, 1940.

26. (a) Levine, P., and Katzin, E. M.: Isoimmunization in Pregnancy and the Varieties of Isoagglutinins Observed, *Proc. Soc. Exper. Biol. & Med.* **45**:343, 1940.

(b) Levine, P.; Katzin, E. M., and Burnham, L.: Atypical Warm Isoagglutinins, *ibid.* **45**:346, 1940.

back to the fetus then agglutinated and destroyed the fetal erythrocytes.

By this time it was evident that the Rh factor in human cells was of definite clinical significance in its relationship to reactions to intragroup transfusions and to erythroblastosis. For the first time it became possible (by using Rh-negative blood) to give transfusions safely to the majority of the patients who had previously had reactions to intragroup transfusions. The fact that pregnancy could stimulate immunization and make possible a reaction to a first transfusion was also realized.

The large volume of work performed by subsequent investigators has almost without exception corroborated the fundamental concepts of Levine, Wiener and their associates.

PRESENT STATUS OF THE RH FACTOR

The Rh Antigen.—The Rh factor is an antigen present on the surface or within the substance of some human erythrocytes. Wiener³⁴ has suggested that it lies partially beneath the surface in contrast to the more superficially located A, B, M and N.³⁵ It was originally thought to be present only in erythrocytes,³⁶ but subsequently it was found in liver, kidney, spleen and salivary gland.³⁷ It is absent from or present in only extremely small amounts in body fluids. It appears early in fetal life and has been demonstrated in a fetus of 17 cm. by Bornstein and Israel.³⁸ Koucky³⁹ has demonstrated anti-Rh agglutinins in the mother during the twelfth week of pregnancy, and in the older literature⁴⁰ there

are several accounts of reactions to intragroup transfusions given for hemorrhages resulting from tubal pregnancies. The previous obstetric history is not recorded in any of these cases, and it is possible that the production of agglutinins had first occurred in a previous pregnancy; if this is true, it need not necessarily indicate that the Rh antigen was present in the cells of the embryo prior to the time the presence of agglutinins was first demonstrated.

The antigenic potency appears high in some instances, although there is great individual variation. Levine⁴¹ stated that 90 per cent of all accidents in intragroup transfusions are due to the Rh factor. Although this may be true, relatively few cases have been reported in which symptoms can be attributed to the antigenic action of this substance (table 7). The smallness of the number may be due partly to lack of investigation or partly to the assignment of reactions to complicating conditions instead of to hemolysis.⁴² However, several fairly extensive reports⁴³ covering many thousand transfusions show few reactions which could possibly be due to immunization to the Rh factor. With the establishment of blood banks and the consequent greater availability of blood, more patients may receive multiple transfusions and the number of reactions may increase.

It is probable that red blood cells must be intact in order to exert an antigenic effect, although Kariher⁴⁴ has stated the belief that the molecular components of fragmented cells may retain their antigenic capacity. At the present time there is no experimental support for this contention. The cells, as far as is known, must be introduced directly into the circulating blood before they can act as antigens, although to date there has been no formal report of attempted immunization by intramuscular, subcutaneous or other routes. The two ways in which the antigen

34. Wiener, A. S., cited by Hooker, S. B.: Isoimmunization in Relation to Intragroup Hemolytic Transfusion Reactions, *New England J. Med.* **225**:871, 1941.

35. However, Wiener, Sonn and Belkin (The Nature of the Rh Agglutination Reaction, Science, to be published), from recent observations, suggest that the explanation of the peculiarities of the Rh reaction is that there are far fewer Rh haptens than A and B haptens per red blood cell.

36. (a) Wiener, A. S., and Forer, S.: A Human Serum Containing Four Distinct Isoagglutinins, *Proc. Soc. Exper. Biol. & Med.* **47**:215, 1941. (b) Levine, P., and Katzin, E. M.: Pathogenesis of Erythroblastosis Fetalis: Absence of the Rh Factor from Saliva, *ibid.* **48**:126, 1941.

37. Boorman, K. E., and Dodd, B. E.: The Group-Specific Substances A, B, M, N and Rh: Their Occurrence in Tissues and Body Fluids, *J. Path. & Bact.* **55**:329, 1943.

38. Bornstein, S., and Israel, M.: Agglutinogens in Fetal Erythrocytes, *Proc. Soc. Exper. Biol. & Med.* **49**:718, 1942.

39. Koucky, R. W.: Experiences with the Rh Substance in Transfusion Reactions, *Minnesota Med.* **26**:980, 1943.

40. Bordley, J.: Reactions Following Transfusion of Blood with Urinary Suppression and Uremia, *Arch. Med.* **47**:288 (Feb.) 1931.

41. Levine, P.: The Pathogenesis of Erythroblastosis Fetalis and Related Conditions, *Cincinnati J. Med.* **23**:596, 1943.

42. Wiener, A. S.: Hemolytic Transfusion Reactions: Diagnosis with Special Reference to the Method of Differential Agglutination, *Am. J. Clin. Path.* **12**:189, 1942.

43. (a) Erf, L. A., and Jones, H. W.: Experiences Associated with a Transfusion Unit in a 700 Bed Hospital: An Animal Survey of Over 3,500 Administrations of Blood and Plasma (Dried), *Ann. Int. Med.* **19**:1, 1943. (b) Mollison, P. L.: The Investigation of Haemolytic Transfusion Reactions, *Brit. M. J.* **1**:529 and 559, 1943. (c) Wiener, A. S.; Oremland, B. H.; Hyman, M. A., and Samwick, A. A.: Transfusion Reactions: Experiences with More Than 3,000 Blood Transfusions, *Am. J. Clin. Path.* **11**:102, 1941.

44. Kariher, D. H.: Erythroblastosis Fetalis (Hemolytic Disease of the Newborn) Occurring in One of Two Twins, *J. A. M. A.* **122**:943 (July 31) 1943.

is ordinarily introduced into a foreign host are by blood transfusion and by the passage of fetal blood into the maternal circulation from the vessels in the placental villi.

Anti-Rh Agglutinins.—Antibodies formed in response to the Rh antigen act as agglutinins in vitro and as hemolysins within the body. Wiener and Peters²⁸ stated that even though serum was freshly activated by the addition of complement no hemolysis could be obtained in vitro. This is surprising in view of the fact that hemolysis is practically always preceded by agglutination⁴⁵ and that an easily performed laboratory experiment consists in agglutinating erythrocytes with appropriate serums and subsequently hemolyzing them by the addition of complement. Koucky³⁹ postulated the production of several types of Rh antibodies, including agglutinins, hemolysins, precipitins, cytotoxins and others; none have been demonstrated except the agglutinin-hemolysin.

Anti-Rh agglutinins are not normally present in the human body, and when demonstrated they have been, with one possible exception,⁴⁸ passively transmitted or have resulted from the antigenic action of artificially introduced cells. Antibodies against Rh-positive cells cannot develop in a person with Rh-positive blood, and Rh antibodies are never present in such persons except in those rare instances in which an infant with Rh-positive blood has agglutinins transferred to it through the placenta.⁴⁷ Free Rh-positive cells may be found in the circulation of a person with Rh-negative blood after the transfusion of Rh-positive blood; because of this phenomenon a person with Rh-negative blood may be incorrectly classified as having Rh-positive blood immediately after transfusion.

When Rh-positive cells enter the circulation of a person with Rh-negative blood, antibodies against the Rh-positive cells may be formed. The response depends on the antigenic potency of the cells introduced and the ability of the recipient to produce immune bodies. Some cells are poor in antigenic quality and some persons are poor reactors to antigenic stimuli; under such conditions no immunization occurs. On the other hand, if both factors in the antigen-antibody reaction are high immunization may develop rapidly.

45. (a) Moss, W. L.: Studies on Isoagglutinins and Isohemolysins, *Bull. Johns Hopkins Hosp.* **21**:63, 1910. (b) Irsigler, F. J.: Urämie nach Bluttransfusion, *Zentrabl. f. Chir.* **58**:1682, 1931.

46. Diamond, L. K.: Hemolytic Transfusion Reactions Due to the Rh Factor: A Preventable Danger, *New England J. Med.* **227**:857, 1942.

47. (a) Boorman, K. E.; Dodd, B. E., and Mollison, P. L.: Clinical Significance of the Rh Factor, *Brit. M. J.* **2**:535 and 569, 1942. (b) Diamond, L. K.: Personal communication to the author.

The amount of blood and the number of injections necessary to cause production of antibodies have not been definitely established and are probably subject to considerable variation. In women who have never been pregnant and in men, at least two transfusions have preceded practically all the reactions for which it seems probable that anti-Rh agglutinins were responsible; usually there have been many more preceding transfusions. Dacie and Mollison,⁴⁸ however, have reported finding anti-Rh agglutinins in Rh-negative blood after a single transfusion. The patient had had one pregnancy; the child had Rh-negative blood. In 7 patients who had received multiple transfusions studied by Koucky,³⁹ antibodies developed within four to thirty-three days after the first transfusion. The patients had been given 500 to 2,200 cc. of blood. The shortest interval for immunization was exhibited by a patient who was four months pregnant, in whom a reaction developed on the fourth day, with the third transfusion. In 10 nonpregnant patients observed by Vogel, Rosenthal and Levine,⁴⁹ reactions occurred twenty-one days to twenty months after the first transfusion. Most of the patients had had many intervening transfusions.

Up to the present time many more accidents due to transfusions following pregnancy than following previous transfusions have been reported. Immunization produced by pregnancy gives a higher and more sustained titer of anti-Rh agglutinins than that produced by transfusion alone⁴⁶; it is probable that the frequent introduction of small amounts of blood from the placenta initiates a greater response than does the introduction by transfusion of larger amounts of blood at greater intervals.

Levine⁵⁰ recently reported obtaining agglutinins in rabbits after fourteen daily injections of 2 cc. of a 1:5,000 suspension of human blood. This, he stated, would be equivalent to the administration of 0.0672 cc. of red blood cell sediment to a 120 pound (54.5 Kg.) woman, and he concluded that since the placental villi have such a great surface area it is probable that immunizing doses of red blood cells escape into the maternal circulation during all pregnancies. If this were true, the only women with Rh-negative blood who would escape immunization

48. Dacie, J. V., and Mollison, P. L.: Survival of Normal Erythrocytes After Transfusion to Patients with Familial Hemolytic Anemia, *Lancet* **1**:550, 1943.

49. Vogel, P.; Rosenthal, N., and Levine, P.: Hemolytic Reactions as a Result of Isoimmunization Following Repeated Transfusions of Homologous Blood, *Am. J. Clin. Path.* **13**:1, 1943.

50. Levine, P.: The Pathogenesis of Erythroblastosis Fetalis: A Review, *J. Pediat.* **23**:656, 1943.

by a fetus with Rh-positive blood would be those incapable of forming antibodies against the fetal cells.

The concentration of agglutinins in the blood is rarely high, and commonly the titer is only 1:4 or 1:8. One of the highest titers recorded⁵⁰ was 1:5,000, present six days after the termination of pregnancy. The comparison of titers obtained by different laboratories is difficult because of the great variation in the agglutinability of the cells used in the determination of the titer. Erythrocytes exhibiting strong agglutinability may give a titer several times greater than that obtained by the use of weakly reacting cells.

Agglutinins may not be demonstrable by any laboratory method and yet may make their presence known by producing reactions to transfusions or erythroblastosis. They may, on the other hand, become demonstrable at any time after a transfusion or during pregnancy; if they are associated with pregnancy, they may show a progressive rise as long as the fetus is within the uterine cavity. Occasionally the titer continues to rise for a few days after the birth of an infant with erythroblastosis, and at times agglutinins which were nondemonstrable during pregnancy and the immediate postpartum period may be present one to two weeks later. Boorman, Dodd and Mollison^{47a} were able to demonstrate agglutinins seven to twenty-one days after delivery more commonly than at any other time.

Subsequent to the assault which originally produces the agglutinins or which stimulates their further production, the titer usually falls and agglutinins may be nondemonstrable within a few months. They may, however, persist for many years; Race, Taylor, Cappell and McFarlane⁵¹ reported finding agglutinins eight years after the last gestation, and Newton and Tebbutt⁵² observed a reaction from a first transfusion fourteen years after the last preceding pregnancy.

The concentration of agglutinins has little relation to their persistence; the serum, mentioned by Koucky,³⁹ which soon after delivery had a titer of 1:5,000 is stated to have contained no agglutinins three months later.

Agglutinins may be temporarily absent after the introduction of Rh-positive blood because all circulating antibodies have united with the newly introduced Rh-positive cells. Wiener²⁸ called this a negative phase. Subsequent examinations,

three to five days later, will usually again reveal agglutinins in the circulation.

When antibodies cannot be demonstrated (except immediately after a transfusion), it is believed that they are held in the reticuloendothelial system or some other part of the body ready to be released by appropriate stimulation.

Antibodies in general appear capable of passing through the normal placenta. This ability has been best demonstrated in relation to the passage of diphtheria antitoxin⁵³ and syphilitic reagins.⁵⁴ Anti-Rh agglutinins likewise pass through the placenta and enter the body of the fetus. In most instances they seem to be removed from the circulation rapidly, but Boorman, Dodd and Mollison^{47a} were able to demonstrate anti-Rh agglutinins in the blood of a pair of Rh-positive twins, both of whom died of erythroblastosis soon after delivery, and Diamond^{47b} observed anti-Rh agglutinins in several infants within a short time after birth.

Many antibodies are known to pass through the breast into the colostrum and milk. The presence of Rh antibodies in breast milk was demonstrated in 3 cases by Witebsky, Anderson and Heide⁵⁵ and in 2 cases by Potter and Davidsohn.⁵⁶ Although little is known of the action of gastric juices on antibodies, it may be possible that agglutinins derived from breast milk are at times the cause of progressive neonatal anemia.

Relation to Sex and to other Antigenic Substances in Blood.—The presence of the Rh factor is entirely unrelated to sex or to the existence of any other known character of human blood.⁵⁷ Agglutinins against Rh, like those against M and N, are never normally present (anti-N agglutinins have never been observed, and anti-M

53. (a) Ruh, H. O., and McClelland, J. E.: Comparison of Diphtheria Immunity in the Mother and in the New-born, *Am. J. Dis. Child.* **25**:59 (Jan.) 1923. (b) Rothholz, A., and Kuttner, A. G.: Comparison of the Schick and the Dick Test in Mothers and New-born Infants, *ibid.* **47**:555 (March) 1934. (c) Cooke, J. V., and Sharma, B. M.: Schick Test in the Newly Born, *ibid.* **44**:40 (July) 1932.

54. Wiener, A. S., and Silverman, I. J.: Permeability of the Human Placenta to Antibodies, *J. Exper. Med.* **71**:21, 1940.

55. (a) Witebsky, E.; Anderson, G. W., and Heide, A.: Demonstration of Rh Antibody in Breast Milk, *Proc. Soc. Exper. Biol. & Med.* **49**:179, 1942. (b) Witebsky, E., and Heide, A.: Further Investigations on the Presence of Rh Antibodies in Breast Milk, *ibid.* **52**:280, 1943.

56. Potter, E. L., and Davidsohn, I.: Unpublished data.

57. Landsteiner, K., and Wiener, A. S.: Studies on an Agglutinin (Rh) in Human Blood Reacting with Anti-Rhesus Sera and Human Isoantibodies, *J. Exper. Med.* **74**:309, 1941.

51. Race, R. R.; Taylor, G. L.; Cappell, D. F., and McFarlane, M. N.: The Rh Factor and Erythroblastosis Foetalis: An Investigation of Fifty Families, *Brit. M. J.* **2**:289, 1943.

52. Newton, N. C., and Tebbutt, A. H.: A Fatal Blood Transfusion Reaction Apparently Due to the Rh Factor, *M. J. Australia* **2**:109, 1943.

agglutinins have been recorded only five times),⁵⁸ but, unlike M and N, Rh is definitely antigenic. It is unlike A and B, since the appropriate isoagglutinins against A and B are normally present in all persons who lack one or both of these characters. Normal isoagglutinins against the Rh factor have never been reported, with the possible exception of 1 case in which the patient was a 5 year old child.⁴⁶ Unlike A and B but like M and N the Rh antigen is present in saliva in only extremely small amounts. All of the antigens mentioned (A, B, M, N and Rh) appear to be present in liver, kidney and salivary gland.³⁷

Subgroups of the Rh Agglutinin and Agglutininogen.—The Rh factor is not a single uniform antigen that is constant in its action. In early studies it became evident that some variation existed. Anti-Rh agglutinins present in the serums of different persons gave fairly uniform reactions with the majority of blood cells, but with a few they gave reactions which were dissimilar both qualitatively and quantitatively.

Wiener has been more active than any other investigator in an attempt to group the types of blood into specific categories according to their responses to the anti-Rh agglutinins present in various human and animal serums. It is interesting to note the increasing complexity of his nomenclature as more and more variability has been discovered. Early in his work studies were described⁵⁷ in which not all cells gave a uniform response to all serums being used. When the first serum that gave positive reactions with only 70 per cent of the samples of blood was encountered, he stated that the antibody demonstrated in case 4 of his series was not the standard Rh agglutinin but an Rh-like antibody.²⁸ Slightly later, in a study of the American Indians, a similar serum is spoken of as demonstrating "a variant of Rh."⁵⁹ On the basis of these observations Wiener soon came to the conclusion⁶⁰ "that there are at least two sorts of Rh agglutininogen, analogous, for example, to the two major varieties of A agglutininogen, A₁ and A₂. It is evident that the special anti-Rh serum tentatively may be compared in its behavior to the anti-A₁ serum which can be prepared by absorbing B serum with A₂ cells. Accordingly, bloods agglutinated by this special anti-Rh₁ serum as well as the standard anti-Rh serum, can be

designated as Rh₁, while bloods agglutinated only by standard anti-Rh sera are designated as Rh₂. As has already been pointed out, about 85 per cent of all white individuals are Rh-positive, and of these approximately one-sixth belong to subtype Rh₂." He also stated in the same paper, "Levine has shown that by absorbing certain anti-Rh sera with Rh₂ blood, a reagent can be obtained which gives reactions parallel to anti-Rh₁ sera." Wiener finally decided that an almost complete analogy existed between the types of the Rh factor and those of the A factor.

Levine⁶¹ about the same time (1942) reported that he, Landsteiner and Wiener had agreed on terminology. The serum which agglutinated cells from 85 per cent of the population was called anti-Rh₁, and that agglutinating cells from 73 per cent, anti-Rh₂. A third serum, which agglutinated 87 per cent of all blood, was designated anti-Rh_{1,2} because it was believed to have antibodies of two types, whereas Rh₁ and Rh₂ each had antibodies of a single type.

Wiener⁶² early in 1943 used this system of nomenclature, though by that time he had concluded that the Rh factor was much more complicated in its behavior than agglutininogen A and that the resemblance was only superficial. He stated that from studies of distribution of the Rh factor it seemed necessary to postulate the existence of three qualitatively different agglutinogens instead of only two, one reacting with anti-Rh₁ serum but not with anti-Rh₂, a second reacting with anti-Rh₂, but not with anti-Rh₁, and a third reacting with both anti-Rh₁ and anti-Rh₂ serums.

Later in the same year he and Landsteiner⁶³ in another paper declared that "in place of the nomenclature suggested by one of the writers,⁶² the following less complicated designations are now suggested. When a distinction between the various subtypes of Rh is desired, the great majority of bloods, namely, those which react also with serum no. 2 of the table (anti-Rh₁ serum), are designated as Rh₁. Of these, a small percentage fail to react with guinea pig antisera or human sera listed as No. 1 and are designated as Rh₁. Those bloods which do not react with sera anti-Rh₁ (No. 2) are called Rh₂. The agglutinins are named so as to correspond to agglutinogens of the blood cells."

58. Davidsohn, I., and Toharsky, B.: The Rh Blood Factor: An Antigenic Analysis. *Am. J. Clin. Path.* **12**:434, 1942.

59. Landsteiner, K.; Wiener, A. S., and Matson, G. A.: Distribution of the Rh Factor in American Indians, *J. Exper. Med.* **76**:73, 1942.

60. Wiener, A. S.: Hemolytic Transfusion Reactions: III. Prevention with Special Reference to the Rh and Cross-Match Tests, *Am. J. Clin. Path.* **12**:302, 1942.

61. Levine, P.: The Rh Factor in Erythroblastosis and Transfusion Accidents, *Proc. New York State A. Pub. Health Lab.* **22**:42, 1942.

62. Wiener, A. S.: Blood Groups and Transfusions, ed. 3, Springfield, Ill., Charles C Thomas, Publisher, 1943.

63. Wiener, A. S., and Landsteiner, K.: Heredity of Variants of the Rh Type, *Proc. Soc. Exper. Biol. & Med.* **53**:167, 1943.

Hardly was the ink on this paper dry when the discovery of another serum, which agglutinated only 30 per cent of cells with which it was tested, led Wiener⁶⁴ to propose still another system of classification. He decided to "designate the new agglutinin as anti-Rh₂ and the agglutino-gen detected by it as Rh₂. Thus, type Rh₁ is now subdivided into type Rh₁ Rh₂ (positive with anti-Rh₂ serum), and type Rh₁ proper (negative with anti-Rh₂ serum), while type Rh₂ is subdivided into type Rh₂ proper (positive with anti-Rh₂ serum) and Rh₂ (negative with anti-Rh₂ serum). In the so-called Rh-negative type there are rare bloods agglutinated

TABLE 1.—*Classification of the Types and Subtypes of Blood in Relation to the Rh Factor, According to Wiener and Landsteiner⁶³*

Designation of Agglutinin in the Serum	Positive Reactions, Approximate %	Reactions of Bloods from White Persons (New York City)			
		About 70%	About 3%	About 14%	About 13%
1. Anti-Rh.....	84	Positive	Negative	Positive	Negative
2. Anti-Rh ₁	73	Positive	Positive	Negative	Negative
3. Anti-Rh ₂	87	Positive	Positive	Positive	Negative
Designation of types.....		Rh positive			Rh negative
Designation of main subtypes		Rh ₁		Rh ₂	
		Rh'			

by the anti-Rh₂ serum. It is obvious that such individuals should now be deleted from the Rh-negative type, because the use of their blood for patients actively or passively sensitized to the Rh₂ agglutino-gen might prove disastrous."

In subsequent papers⁶⁵ eight types of blood were described that were identified by their reaction to the three types of testing serums which Wiener recognized; anti-Rh serum agglutinated the blood of approximately 85 per cent, anti-Rh₁ agglutinated that of about 70 per cent, and anti-Rh₂ agglutinated that of about 35 per cent of white persons.

Early in 1944 Wiener, Sonn and Belkin⁶⁶ gave further evidence of the existence of these types in a statistical analysis of the reactions to the Rh factor exhibited by the blood of 275 children in 97 families.

Although the majority of anti-Rh serums seem to fall in one of three groups, it is probable that

an attempt to include all minor varieties in a system of nomenclature will never be feasible. Gallagher and Jones⁶⁷ described three serums, one from guinea pigs giving positive reactions with the blood of 83 per cent of all persons tested, one human serum giving positive reactions with 84 per cent and a second human serum giving positive reactions with only 54 per cent of those tested. Fisk and Foord⁶⁸ studied four serums giving positive reactions with 83.0 per cent, 84.9 per cent, 86.0 per cent and 87.2 per cent of bloods respectively. A few cells reacted positively to one or another of these serums reacting negatively to guinea-pig serums, but for the most part animal and human serums gave similar results. They found, however, that of 312 cord bloods all of which gave positive reactions to guinea-pig serum, 8.8 per cent gave negative reactions with one human serum and 13.6 per cent with another human serum. The uniform agglutination of cord blood by animal serum has been subsequently corroborated by Wiener, Sonn and Belkin,⁶⁶ and it seems that animal serum is useless for typing the blood of infants at the time of birth. All specimens of cord blood showed much stronger agglutination in guinea pig serum than did adult cells.

It was originally believed that rabbit agglutinins produced against rhesus cells were identical with the anti-Rh agglutinins present in human blood. It has been definitely shown, however, that there are other differences besides the one just mentioned. Animal agglutinins act on about 85 per cent of adult human cells, and their activity parallels that of anti-Rh serum fairly closely, but Davidsohn and Toharsky⁶⁹ found that adsorption of human anti-Rh serum with human Rh-positive cells removed all of the agglutinins for monkey cells but only part of those for human cells.⁶⁹ Also, when human anti-Rh serum was adsorbed by monkey cells, the agglutinins for monkey cells were removed but not those for human blood. When animal serum produced by inoculation of guinea pigs with monkey blood was adsorbed by monkey cells, the agglutinins for for both monkey and human blood were completely removed, but when it was adsorbed with human cells the agglutinins for monkey cells were unaffected.

67. Gallagher, F. W., and Jones, L. R.: Preparation and Use of Rh Testing Sera, *J. Immunol.* **46**:9, 1943.

68. Fisk, R. T., and Foord, A. G.: Observations on the Rh Agglutino-gen of Human Blood, *Am. J. Clin. Path.* **12**:545, 1942.

69. The reaction was dependent on the kind of Rh-positive cells used, and it was similar to that demonstrated by Levine in the experiments in which he was able to adsorb one antibody from serum giving positive reactions with the blood of 87 per cent of persons tested and have another antibody left.

64. Wiener, A. S.: Distribution and Heredity of Variants of the Rh Type, *Science* **98**: 82, 1943.

65. (a) Wiener, A. S.: Genetic Theory of the Rh Blood Types, *Proc. Soc. Exper. Biol. & Med.* **54**:316, 1943. (b) Wiener, A. S.; Sonn, E. B., and Belkin, R. B.: Heredity and Distribution of the Rh Blood Types, *ibid.* **54**:238, 1943.

66. Wiener, A. S.; Sonn, E. B., and Belkin, R. B.: Heredity of the Rh Blood Types, *J. Exper. Med.* **79**: 235, 1944.

General Distribution of the Rh Factor.—Of 11,261 unselected white persons examined in the United States, Germany, England, Wales, Australia and Chile, 84.2 per cent had blood which was Rh-positive and 15.8 per cent had Rh-negative blood (table 2). Human serums reacted with a slightly higher percentage of blood cells than did animal serums, but in general the two gave similar results. Only standard anti-Rh serums were used.

Studies on Negroes,⁷⁰ American Indians⁵⁹ and Chinese⁷¹ living in the United States revealed a higher incidence of Rh-positive blood in persons of these races (table 3) than in white persons in the same areas. The difference was especially notable in the full-blooded Indians and the Chinese. Only 1 person with Rh-negative

can Indians of mixed parentage showed an incidence approximating that which would be expected on the basis of 60 per cent white blood, if one considers the incidence of Rh-positive blood in white persons as 85 per cent and in Indians as 100 per cent.

Vaccaro⁷² found that only 7.5 per cent of 119 Chilean men and women had Rh-negative blood. Although this is a small group on which to base a conclusion, it may be possible that further studies will show a higher incidence of Rh-positive blood in Chileans than in any previously reported white population.

When the reaction to the anti-Rh serum agglutinating the blood of 70 to 73 per cent of white persons was investigated in Negroes, Indians and Chinese, an unexpected divergence

TABLE 2.—Incidence of the Rh Factor in the Blood in White Populations

Author	Country	Total Number of Subjects	Blood Tyre				Source of Testing Serum
			Rh+		Rh-		
			No.	%	No.	%	
Levine ⁶⁰	United States	1,035	897	86.6	138	13.4	Human
Wiener ⁶⁰	United States	777	665	85.6	112	14.4	Animal and human
Fisk and Foord ⁶⁸	United States	927	788*	85.0	139*	15.0	Animal
Gallagher and Jones ⁶⁷	United States	156	150*	95.0	26*	17.0	Animal
Gallagher and Jones ⁶⁷	United States	118	100*	85.0	18*	15.0	Human
Boorman ^{47a}	England	1,610	1,371	85.15	239	14.85	Human
Hoare ^{136a}	Wales	1,122	949.	84.6	173	15.4	Animal
Simmons, Graydon, Jakobowicz and Bryce ¹³⁵	Australia	3,641	2,958	82.34	643	17.66	Human
Dahr ^{136b}	Germany	1,756	1,475*	84.0	281*	16.0	Animal
Vaccaro ⁷²	Chile	119	110*	92.5	9*	7.5	
Total		11,261	9,483	84.2	1,775	15.8	

* Figures calculated from authors' data.

TABLE 3.—Racial Differences in Reaction to Standard Anti-Rh Serum of the Type Agglutinating the Cells of Eighty-Five per cent of White Persons

Author	Race	Total Number of Subjects	Reaction to Anti-Rh Serum			
			Positive		Negative	
			No.	%	No.	%
Combined data	White	7,620	6,485	85.1	1,135	14.9
Landsteiner and Wiener ⁵⁷	Negro	113	104	92.0*	9	8.0*
Levine ^{70b}	Negro	264	252*	95.5	12*	4.5
Landsteiner, Wiener and Matson ⁵⁹	American Indian					
	Full blooded	120	119	99.2	1	0.8
	Mixed blooded	155	148	95.5*	7	4.5*
Levine and Wong ⁷¹	Chinese	150	149	99.3	1	0.7

* Figures calculated from authors' percentages.

blood was found among 120 Indians examined and only 1 among 150 Chinese. It may be possible that these two persons had some intermixture of white blood; that Indians and Chinese may uniformly have Rh-positive blood. Ameri-

70. (a) Landsteiner and Wiener.⁵⁷ (b) Levine, P.: On Human Anti-Rh Sera and Their Importance in Racial Studies, *Science* **96**:452, 1942.

71. Levine, P., and Wong, H.: The Incidence of the Rh Factor and Erythroblastosis Fetalis in Chinese, *Am. J. Obst. & Gynec.* **45**:832, 1943.

was revealed (table 4). The blood of Negroes and Indians yielded a much lower percentage

TABLE 4.—Racial Differences in Reaction to Anti-Rh₁ Serum*

Author	Race	Total Number of Subjects	Reaction of Blood	
			Posi- tive, %	Nega- tive, %
Wiener ⁵⁸	White	68	70	30
Levine et al. ^{51b}	White	334	73	27
Levine ^{70b}	Negro	118	46	54
Landsteiner, Wiener and Matson ⁵⁹	American Indian			
	Indian	69	58	42
Levine and Wong ⁷¹	Chinese	150	93	7

* All serums used in these determinations were of the type agglutinating the cells of approximately 70 per cent of white persons.

of positive reactions, while that of the Chinese reacted almost as uniformly to this serum as to the other. This suggests a definite qualitative difference in the antigenic components of the cells which react to these two serums.

The present proportion of persons with Rh-positive and with Rh-negative blood in the white race and in other races is a matter of interest. Differences in the distribution of the blood groups

72. Vaccaro, H.: Hemoagglutinogeno Rh y eritroblastosis foetalis, *Rev. chilena de pediat.* **14**:717, 1943.

in different races have been attributed to the effects of geographic location, such as isolation of small groups of people with consequent inbreeding and increasing predominance of certain groups and migration of specialized races resulting in intermixture of characteristics and to mutation from the 0 form after the establishment of races. Wiener⁷³ called attention to the fact that in order to produce the incidence of Rh-negative blood which exists in the white race, the rate of mutation from Rh-positive to Rh-negative would have to be much higher than that of any other mutation previously described. He concluded that the incidence could be explained best on the basis of intermixture of races which originally consisted largely of persons with Rh-positive or of persons with Rh-negative blood. Haldane⁷⁴ also mentioned this as a reasonable possibility. Hogben⁷⁵ recently stated that he believed the rate of mutation would not have to be inordinately high if it was interpreted as a mutation at the Rh locus from any one of a series of five or more dominant alleles. Fisher, Race and Taylor⁷⁶ have taken exception to this view and have stated that it is unjustified.

Inheritance of the Rh Factor.—The Rh factor appears to be inherited in a mendelian manner. Before subgroups of Rh had been recognized, or before it was possible to differentiate them, Landsteiner and Wiener⁵⁷ and Wiener and Sonn⁷⁷ determined the number of persons with Rh-positive and with Rh-negative blood in 100 families with 475 children and found a close correlation between the number observed in each group and the number to be expected on the basis of mendelian inheritance. They concluded that inheritance was by means of two allelic genes, Rh and rh, Rh representing the positive character and being dominant over rh, the negative character. Thus the two genotypes RhRh and Rhrh would be included in the phenotype Rh +, while only the genotype rh rh could occur with the phenotype Rh —. Two persons of the phenotype Rh + may have offspring with Rh-negative blood, but 2 persons of the phenotype Rh — cannot have children with Rh-positive blood. In a population of which 84.8 per cent of the persons are of the phenotype Rh +, 36.9

per cent will be RhRh, 47.7 per cent Rhrh and 15.4 per cent rh rh in genotype. If mating is random, 13.1 per cent of all marriages will be between women of the phenotype Rh — and men of the phenotype Rh + and in 9.36 per cent of all pregnancies a woman of the genotype rh rh will carry a child of the genotype Rh rh.⁷⁴

After the discovery that some serums were capable of agglutinating the blood of only 70 per cent instead of 85 per cent of all persons, Wiener and Landsteiner⁶³ and Wiener⁶⁴ stated that the ability of cells to be agglutinated by one or the other of these serums also appeared to follow a definite mendelian pattern of inheritance. According to the terminology used at that time inheritance was by means of three allelic genes, Rh₁, Rh₂ and rh. Rh₁ (the gene for the antigen agglutinable by the serum reacting with 70 per cent of all cells but not by that reacting with 85 per cent of all cells), and both Rh₁ and Rh₂ were believed to be dominant over rh. The antiserum which gave a positive reaction with the blood of 87 per cent of the persons tested was believed to isolate a third type of antigen (called Rh₁₂ by Levine); subsequently, therefore, four allelic genes, three Rh genes and one rh, were postulated.⁶² The serum found later to agglutinate the cells of only 30 per cent of the persons tested was stated to identify still another variety of Rh antigen, which also followed a definite pattern of inheritance. By the use of this serum in addition to the others previously described, Wiener^{65a} and Wiener, Sonn and Belkin^{65b} decided that there were six allelic genes, all of equal dominance, and designated them Rh₁, Rh₂, Rh, Rh', Rh'' and rh (table 5). A study by the latter authors⁶⁶ of 97 families with 275 children showed no discrepancies in inheritance according to the theory of 6 alleles.

A group of English investigators, Race, Taylor, Boorman and Dodd,⁷⁸ have observed, in independent investigations, much the same results obtained by Wiener and his associates. They have found two serums each of which agglutinates the cells of 30 per cent of the persons tested. These have been designated K and J and appear to correspond to the anti-Rh₂ serum of Wiener.

Another serum, St, dissimilar to any as yet reported by Wiener, was observed by Race and Taylor.⁷⁹ It agglutinates all Rh-negative blood and Rh-positive blood from persons who are heterozygous and from about 20 per cent of those who appear to be homozygous. They and their col-

73. Wiener, A. S.: The Rh Factor and Racial Origins, *Science* **96**:407, 1922.

74. Haldane, J. B.: Selection Against Heterozygosis in Man, *Ann. Eugenics* **11**:333, 1943.

75. Hogben, L.: Mutation and the Rhesus Reaction, *Nature, London* **152**:721, 1943.

76. Fisher, R. A.; Race, R. R., and Taylor, G. L.: Mutation and the Rhesus Reaction, *Nature, London* **153**:106, 1944.

77. Wiener, A. S., and Sonn, E. B.: Heredity of the Rh Factor, *J. Genetics* **45**:157, 1943.

78. Race, R. R.; Taylor, G. L.; Boorman, K. E.; and Dodd, B. E.: Recognition of Rh Genotypes in Man, *Nature, London* **152**:563, 1943.

79. Race, R. R., and Taylor, G. L.: A Serum That Discloses the Genotype of Some Rh Positive People, *Nature, London* **152**:300, 1943.

laborators⁸⁰ have postulated that persons whose blood fails to react with this serum are of the genotype Rh_1Rh_1 , and they have stated that with the use of this serum in addition to the others previously recognized, the Rh genotype of at least 80 per cent of the population can be determined. They have observed the 6 allelomorphs described by Wiener and believe there is a seventh one (Rh_7) which can be discovered only by the use of St serum. Loutit,⁸¹ reviewing the papers by Wiener and Race and their associates, concluded that the investigations were in such close agreement that the varieties of genes described could be accepted as established.

RELATIONSHIP OF THE RH FACTOR TO ERYTHROBLASTOSIS

Diagnosis of Erythroblastosis.—Erythroblastosis fetalis is a disease characterized by the

hemolytic anemia of the fetus and newborn” in order to indicate that hemolysis is the basic phenomenon.

The pathologic manifestations of erythroblastosis are direct results of excessive destruction of erythrocytes and of an attempt on the part of the body to compensate for this loss. Anemia, increased bilirubin in the blood and in various fixed tissues of the body, abnormal erythropoiesis in many organs, including the spleen and liver, and an increase in immature forms of erythrocytes in the circulating blood are among the signs most commonly observed. The extreme edema which is present in many of the infants with more severe erythroblastosis has not been completely explained; factors as to its origin which have been suggested include renal failure, injury of the general capillary bed and a decrease in plasma proteins occurring in conjunction with

TABLE 5.—The Rh Blood Types and Their Theoretic Genotypes (Wiener, Sonn and Belkin^{65b})

Phenotype rh	Reactions with Rh Antiserums					Approximate Frequency in White Persons (New York City), %	Theoretically Possible Genotypes
	Anti-Rh	Anti-Rh ₁	Anti-Rh ₂	Anti-Rh'	Anti-Rh''		
	—	—	—	—	—	12.75	rh rh
Rh ₁	+	+	—	+	±	50	Rh_1Rh_1 Rh_1rh Rh_1Rh' Rh_1Rh'' $Rh'Rh$
Rh ₂	+	—	+	+	+	15.5	Rh_2Rh_2 Rh_2rh Rh_2Rh' Rh_2Rh'' $Rh''Rh$
Rh_1Rh_2	+	+	+	+	+	17	Rh_1Rh_2 Rh_1Rh'' $Rh'Rh_2$
Rh	+	—	—	+	+	2.5	$RhRh$ $Rhrh$
Rh'	—	+	—	+	—	2	$Rh'Rh'$ $Rh'rh$
Rh''	—	—	+	—	+	0.25	$Rh''Rh''$ $Rh''rh$
$Rh'Rh''$ *	—	+	+	+	+	$Rh'Rh''$

* This theoretically possible type has not yet been encountered, which is not surprising considering the extremely low value of the calculated frequency of the genotype $Rh'Rh''$.

abnormal destruction and regeneration of erythrocytes. Until recently there was some disagreement as to which was the primary process,⁸² but it appears fairly certain in view of recent studies that hemolysis initiates all the other pathologic changes. Several authors⁸³ have suggested replacing the name “erythroblastosis” with “acute

cellular hemolysis. The interrelationship of the various pathologic changes has been discussed recently by Davidsohn.⁸⁴

The general symptomatology has been well discussed on several occasions,⁸⁵ and in a typical case the diagnosis of erythroblastosis is easily

80. Race, R. R.; Taylor, G. L.; Cappell, D. F., and McFarlane, M. N.: Recognition of a Further Common Rh Genotype in Man, *Nature*, London **153**:52, 1944.

81. Loutit, J. F.: Human Blood Groups, *Nature*, London **153**:97, 1944.

82. (a) Diamond, L. K.; Blackfan, K. D., and Baty, J. M.: Erythroblastosis Fetalis and Its Association with Universal Edema of the Fetus, Icterus Gravis Neonatorum and Anemia of the Newborn, *J. Pediat.* **1**:269, 1932. (b) Hawksley, J. C., and Lightwood, R.: A Contribution to the Study of Erythroblastosis: Icterus Gravis Neonatorum, *Quart. J. Med.* **3**:155, 1934.

83. (a) Boorman and Dodd.³⁷ (b) Race, Taylor, Cappell and McFarlane.⁵¹ (c) Kariher, D. H., and Spindler, H. A.: Erythroblastosis Fetalis and the Blood Factor Rh, *Am. J. M. Sc.* **205**:369, 1943.

84. Davidsohn, I.: The Rh Factor, *M. Clin. North America* **28**:232, 1944.

85. (a) Diamond, Blackfan and Baty.^{82a} (b) Hawksley and Lightwood.^{82b} (c) Clifford, S. H., and Hertig, A. T.: Erythroblastosis of the Newborn, *New England J. Med.* **207**:105, 1932. (d) Ross, S. G., and Waugh, T. R.: Certain Types of Icterus Gravis, *Am. J. Dis. Child.* **51**:1059 (May) 1936. (e) Potter, E. L., and Adair, F. L.: Fetal and Neonatal Death, Chicago, University of Chicago Press, 1940.

established. The milder forms may be difficult or impossible to diagnose on clinical grounds, and occasionally it may be impossible to establish the diagnosis even at autopsy.⁸⁶ No single feature, including severe unexplained anemia, severe icterus or fetal hydrops,⁸⁷ can be considered pathognomonic, and although the possibility of the disease should be considered whenever any one of these symptoms is present in the fetus or the newborn infant, a definite diagnosis must be made with caution.

Anemia is more constantly present than any other symptom, but icterus almost always develops rapidly if the infant is born alive. The icteric index frequently becomes extremely high, indicating that excessive hemolysis and inability of the liver to eliminate the products of cellular destruction both exist. If the blood of the infant is examined immediately after birth, erythroblasts and normoblasts are usually found, but if smears are not made for several days the immature cells may have disappeared. However, an increase in immature red cells in the peripheral blood when unassociated with other symptoms cannot be considered indicative of erythroblastosis. Casey and Crowson⁸⁸ examined the blood of 116 infants within twenty-four hours after birth and found an appreciable increase in the number of immature cells in 4 infants, all of whom subsequently died. The causes of death were not given, but it can be concluded that the infants did not have erythroblastosis.

Enlargement of the spleen is one of the most significant diagnostic criteria. If the spleen extends 2 cm. or more below the costal margin or weighs 25 Gm. or more, either erythroblastosis or syphilis is almost certain to be the causative factor. In several thousand autopsies on fetuses and newborn infants I have never seen this degree of enlargement from any other cause. If it were necessary to make a diagnosis of erythroblastosis on observation of a single organ or on a single laboratory finding, a study of the spleen would yield the highest percentage of correct results.

Before a definite diagnosis is made, however, the general symptom complex must be present. Although subsequent events (especially the birth of a sibling with definite erythroblastosis) may

show that the disease existed even though the symptoms were incomplete or atypical, it is unjustifiable to diagnose this condition on inadequate grounds. The grave outlook for future child-bearing which exists once the presence of erythroblastosis is established is sufficient reason for making the diagnosis with caution.

Study of the Rh factor in the parents and in the affected child may give contributory evidence of the presence or absence of the disease. Finding that the mother's blood is Rh negative and that the father and the child have Rh-positive blood lends support to the diagnosis, and this is augmented by the demonstration of anti-Rh agglutinins in the maternal blood. Discovering that the mother's blood is Rh positive is strong but not final evidence against erythroblastosis in the infant. Mollison⁸⁹ stated the belief that if no antigen which is lacking in the mother is present in the fetus the diagnosis of erythroblastosis can be practically excluded. The Rh status of the family, however, is never in itself a sufficient basis for making a diagnosis.

It has always been the belief of the author that erythroblastosis should be considered a specific pathologic entity, and this belief has been strengthened by the recent work on the Rh factor. The oft recurring statement that erythroblastosis is due to many conditions and is only a symptom complex associated with various etiologic agents indicates unfamiliarity with the details of the disease complex. Practically any abnormal state characteristic of erythroblastosis can be duplicated by some other condition, but it is unwarranted to say that erythroblastosis is not a disease entity only because erythroblastemia may be found in association with infections, abnormal erythropoiesis in association with syphilis and jaundice in association with internal hemorrhage. Whether the cause is ultimately proved to be an antigen-antibody reaction, as currently believed, or whether some other etiologic agent is eventually discovered, there is a definite condition for which a uniform cause may be expected.

Incidence of Erythroblastosis.—The true incidence of erythroblastosis is somewhat difficult to determine. It can be accurately calculated only in relation to a given number of births, and then only when all macerated as well as nonmacerated fetuses and infants who have died have been examined at autopsy by a pathologist fully aware of the diagnostic criteria of erythroblastosis and when all surviving infants have been under ade-

86. Potter, E. L.: Reducing the Hazards of the First Two Days of Life: The Role of the Rh Factor, *J. Pediat.* **23**:486, 1943.

87. Potter, E. L.: Universal Edema of the Fetus Unassociated with Erythroblastosis, *Am. J. Obst. & Gynec.* **46**:130, 1943.

88. Casey, A. E., and Crowson, S. H.: Nucleated Erythrocytes in Newly Born Infants in Relation to Maternal Rh Compatibility, *Proc. Soc. Exper. Biol. & Med.* **54**:320, 1943.

89. Mollison, P. L.: The Etiology of Erythroblastosis Fetalis and Certain Haemolytic Transfusion Reactions with Special Reference to the Rh Factor, *Proc. Roy. Soc. Med.* **36**:221, 1943.

quate clinical observation. Javert⁹⁰ reported an incidence of 1 per 438 deliveries at the New York Hospital during a five year period ending in 1940; this was a 400 per cent increase over the incidence observed from 1933 to 1936. Potter and Adair⁹¹ reported 1 death from erythroblastosis for each 1,000 deliveries from 1931 to 1941, but they have had an incidence of 1 for each 500 for the years 1941, 1942 and 1943. From 1941 to 1943 inclusive there have been 10,378 births at the Chicago Lying-in Hospital, with loss of 360 fetuses and infants (all fetuses and infants weighing over 400 Gm. are included). A diagnosis of erythroblastosis was made for 22 infants who died or were stillborn. This figure represents 6.1 per cent of the total deaths but only 0.21 per cent of the total births.⁹² The diagnosis was made for 6 additional infants who did not die. This raises the total incidence to 1 per 370 births. During this period postmortem examinations in no way differed from those performed from 1934 to 1941, but infants in the nurseries were more closely scrutinized for the possible presence of erythroblastosis. Studies of the blood were made for all infants who were pale or had early jaundice or who for any reason were doing poorly.

Only 2 of the 28 infants were delivered by women who had not been previously pregnant, which makes the incidence 1 per 2,380 first-born infants and 1 per 245 subsequently born infants. Schwartz and Levine⁹³ reported that in a series of 2,000 deliveries with a considerably greater total fetal and infant mortality 4.4 per cent of the infants who died (0.35 per cent of the infants born) had erythroblastosis. Six additional deaths were considered probably due to erythroblastosis, almost entirely, as far as can be determined, on the basis that the mother had Rh-negative blood. The addition of this case made 8.2 per cent of the deaths due probably to erythroblastosis and increased the incidence of fatal erythroblastosis to 0.65 per cent of the total number of births. This incidence is three times that observed at the Chicago Lying-in Hospital. The authors state that the figures "support Levine's⁹⁴ contention that the incidence of erythroblastosis will be considerably higher if based

on the results of the Rh tests." Many women with Rh-positive blood lose babies from unexplained causes both before and after birth, and it is unreasonable to assume that because a woman has Rh-negative blood the cause of the death of her infant must be related to this fact.

Etiology of Erythroblastosis.—The previously suggested causes of erythroblastosis include maternal toxemia, nephritis, heart disease and anemia, fetal nephritis or renal failure, hepatic dysfunction, malformation of the heart, malformation or neoplasm of hemopoietic tissues, sepsis, syphilis, toxemia or allergy, defect of the primitive germ plasma or abnormality of the zygote, hereditary transmission by a dominant gene or by a recessive gene, abnormal persistence of embryonal hemopoiesis, exhaustion of a passively transmitted maternal hormone necessary for hemopoiesis or the absence of a hormone inhibiting hemolysis, breakdown in the placental barrier resulting in abnormal intermixture of maternal and fetal blood and fetal response to maternal immunization against fetal hemoglobin or against the A or B substance in fetal blood cells.

The present concept of the causation of erythroblastosis is the only one of all those thus far considered which seems adequate. This theory presumes that an antigenic substance, Rh, is absent from the blood of a given woman and present in that of her husband; when conception takes place an Rh-positive sperm fertilizes an Rh-negative ovum and the resulting fetus is of the phenotype Rh +. Fetal blood bearing the Rh antigen escapes from the placenta into the maternal circulation. Immunization of the mother takes place, since the Rh factor is an antigen foreign to her cells. Immune bodies thus produced return to the fetus, react with its Rh-positive cells and destroy them. When the antigen-antibody reaction in the fetus is sufficient to destroy erythrocytes at a proportionately faster rate than the hemopoietic tissue can produce them, the symptoms of erythroblastosis result.

EVIDENCE SUPPORTING THE CONTENTION THAT ERYTHROBLASTOSIS IS AN RH ANTIGEN-ANTIBODY REACTION IN THE FETUS

1. The clinical and pathologic manifestations can all be explained as direct results of hemolysis or as compensatory mechanisms designed to combat the effects of hemolysis. Anemia, icterus and probably edema are direct results of hemolysis; excessive erythropoiesis with associated erythroblastemia, hepatomegaly and splenomegaly are the result of an attempt to replace the hemolyzed cells.

2. The great majority of women giving birth to infants with erythroblastosis have Rh-negative

90. Javert, C. T.: Erythroblastosis Neonatorum: An Obstetrical-Pathological Study of Forty-Seven Cases, *Surg., Gynec. & Obst.* **74**:1, 1942.

91. Potter, E. L., and Adair, F. L.: Clinical-Pathological Study of the Infant and Fetal Mortality for a Ten Year Period at the Chicago Lying-In Hospital, *Am. J. Obst. & Gynec.* **45**:1054, 1943.

92. Potter, E. L.: Unpublished data.

93. Schwartz, H. A., and Levine, P.: Studies on the Rh Factor, *Am. J. Obst. & Gynec.* **46**:827, 1943.

94. Levine, P.: Pathogenesis of Erythroblastosis, *New York State J. Med.* **42**:1928, 1942.

blood. Only 15 per cent of all white women in this country have Rh-negative blood, while of mothers giving birth to infants with erythroblastosis over 90 per cent have Rh-negative blood. This difference is far too great to be due to chance, and a necessary relationship between erythroblastosis and the Rh-negative state of the mother's blood is evident. Of 711 women reported to have given birth to infants with erythroblastosis whose Rh status has been determined, 651 had Rh-negative blood (table 6).

TABLE 6.—*Rh Status of Infants with Erythroblastosis and of the Parents*

	Mother's Blood		Father's Blood		Infant's Blood	
	Rh+	Rh-	Anti-Rh Agglutins	Rh+	Rh-	Rh-
Levine ⁹⁴	35	315	..	204	0	189
Potter et al. ^{96a}	5	55	10	21	1	25
Race et al. ⁹¹	6	44	38
Boorman et al. ⁹⁶	3	97	93
Wiener ⁹²	6	37
Gimson ^{95b}	0	19	18	19
Yaccaro ⁷²	14	14	14	..	14
Javert ¹⁰⁰	3	9
Risk and Poord ⁹⁸	9	6
Diamond ⁹⁶	6	5
Brown and Levine ^{110f}	1	5	..	0
Kariber and Spindler ^{98c}	6	6	6
Mollison ⁹⁹	6	6
Schwartz and Levine ⁹³	6	3
Brewer ^{140b}	5
Hoare ^{130a}	5	5
Witebsky and Heide ^{55b}	2	2	2	..	2
Witebsky et al. ^{56a}	1	1
Damashek et al. ^{140e}	1	1	1
Crawford and Stewart ^{140c}	2	2
Aggaard ^{128a}	2	2
Koucky ⁹⁰	2	2	1
Kariber ⁴⁴	1	1
Newerla ¹⁴⁰ⁱ	1	1
Hertzog ^{98b}	1	1
Total.....	60	951	213	254	1	202
						3

3. Anti-Rh agglutinins can be demonstrated in the circulation of some women giving birth to infants with erythroblastosis. Most of the English investigators⁹⁵ have reported a much higher incidence of agglutinins than has been found by any one in the United States. Boorman, Dodd and Mollison^{47a} found that 44 of 46 patients with Rh-negative blood had agglutinins seven to twenty-one days after delivery. A subsequent report⁹⁶ of 100 women proved to have had infants with erythroblastosis indicates that 97 had Rh-negative blood and that the blood of only 4 of the 97 failed to contain demonstrable anti-Rh agglutinins. In the series studied by

Potter, Davidsohn and Crunden^{96a} the low incidence of 10 patients with blood containing agglutinins in 60 with Rh-negative blood may well be due to the fact that the majority of the tests were made several months or years after the birth of the last child. Levine, Burnham, Katzin and Vogel^{81b} reported the postpartum presence of agglutinins in 41 of 141 women and showed a decreasing incidence with progressive prolongation of the interval between delivery and testing. Of 70 women tested within two months after delivery, 33 had anti-Rh agglutinins in the blood, while agglutinins could be demonstrated in the blood of only 2 of 41 when the interval was in excess of one year. The low incidence of agglutinins may be caused by insufficiently sensitive methods of testing, or it may mean that the antibodies are attached to tissues and become free in the circulation only under special stimulation.

4. Anti-Rh agglutinins are present in the milk of some women who give birth to infants with erythroblastosis. Three cases have been reported by Witebsky, Anderson and Heide⁵⁵ and 2 have been observed by Potter and Davidsohn⁵⁶ in which agglutinins were present in milk. Their presence in the milk has doubtless been demonstrated in additional cases which are unreported, and if proper investigations were made they might well be shown to be present in the milk of a large percentage of women who have a high serum titer of anti-Rh agglutinins.

5. Anti-Rh agglutinins have been found in the circulation of infants with erythroblastosis soon after birth. Twins, both of whom had demonstrable anti-Rh agglutinins in their blood, were observed by Boorman, Dodd and Mollison,^{47a} and Diamond^{47b} states that he has observed the presence of anti-Rh agglutinins on several occasions soon after birth. This is somewhat surprising, for one would expect an antigen-antibody reaction to remove free antibodies from the circulation.

6. Rh-negative blood survives a normal length of time when administered to infants with erythroblastosis. It has been shown⁹⁷ that fresh blood cells introduced into the circulation by transfusion can be identified eighty to one hundred

95. (a) Race, Taylor, Cappell and McFarlane.⁹¹ (b) Gimson, J. B.: Haemolytic Disease of the Newborn (Erythroblastosis Foetalis): Its Treatment with Rhesus-Negative Blood, *Brit. M. J.* **2**:293, 1943.

96. Boorman, K. E.; Dodd, E. E., and Mollison, P. L.: The Incidence of Haemolytic Disease of the Foetus ("Erythroblastosis Foetalis") in Different Families: The Value of Serological Tests in Diagnosis and Prognosis, *J. Obst. & Gynaec. Brit. Emp.* **51**:1, 1944.

96a. Potter, E. L.; Davidsohn, I., and Crunden, A. B.: The Importance of the Rh Blood Factor in Erythroblastosis, *Am. J. Obst. & Gynec.* **45**:254, 1943.

97. (a) Wiener, A. S.: Longevity of the Erythrocyte, *J. A. M. A.* **102**:1779 (May 26) 1934. (b) Mollison, P. L.: Some Revised Principles of Blood Transfusion, *Proc. Roy. Soc. Med.* **36**:335, 1943. (c) Mollison, P. L., and Young, I. M.: In Vivo Survival in the Human Subject of Transfused Erythrocytes After Storage in Various Preservative Solutions, *Quart. J. Exper. Physiol.* **31**:359, 1942.

and twenty days later unless they have been abnormally hemolyzed. When Rh-negative blood is given infants with erythroblastosis the cells are more apt to survive for normal periods than when Rh-positive cells are used. Mollison⁸⁸ reported that when mixtures of Rh-positive and Rh-negative cells were given the Rh-positive cells, except in 1 instance, disappeared almost immediately while the Rh-negative cells were present three months later. If there were no anti-Rh agglutinins present or if there were no relationship of the Rh factor to erythroblastosis, Rh-positive blood should survive as well as Rh-negative.

7. The husbands of practically all women with Rh-negative blood with affected infants and practically all of the affected infants have Rh-positive blood. If there were no relation between the possession of Rh-positive blood by the father and erythroblastosis in the offspring, the husbands of at least 15 per cent of women with Rh-negative blood who have infants with erythroblastosis and almost 60 per cent of the children should have Rh-negative blood. (The incidence of Rh-negative blood in husbands should be the same as that in the general population. All of the children born of these fathers should have Rh-negative blood, and since almost half of the men whose phenotype is Rh + are heterozygous for the Rh factor about half of those born of fathers with Rh-positive blood should also have Rh-negative blood.) Levine⁹⁴ found that all husbands of 204 women with Rh-negative blood who gave birth to babies with erythroblastosis had Rh-positive blood. Occasional husbands and infants with Rh-negative blood have been reported,⁹⁸ but a great preponderance have Rh-positive blood.

8. The disease is rare in first-born children. The almost uniform sparing of first-born children can be explained only on the basis that something transpires during a pregnancy to make conditions appropriate for the development of the disease in children born subsequently. The process of immunization is known to require time, and it is probable that during the course of a single pregnancy an erythroblastosis-producing concentration of antibodies does not ordinarily develop.⁹⁹ An extremely mild form of the disease occurs occasionally in a first child, and a severe

form may exist if the mother has been previously immunized by the introduction of Rh-positive blood by transfusion. However, unless the mother has previously received a transfusion, death from erythroblastosis is extremely rare in the first offspring. It seems clear that the condition responsible for maternal immunization ordinarily occurs prior to the pregnancy in which erythroblastosis is first manifested.

9. Once the disease occurs it is repeated in all subsequently born siblings with Rh-positive blood. The degree and duration of an acquired immunity vary with the potency of the antigen and with the capability of the body to produce antibodies. It seems almost certain that the immunity acquired for the Rh antigen either is permanent or is renewed by some condition inherent in all pregnancies. It is inconceivable that any condition produced by the individual action of a genetic factor, infection or any other known etiologic agent should fail to act in a first pregnancy and be invariably repeated in all subsequent pregnancies. It is likewise untenable that if the action of antibodies lasted for only a short time new antibodies would invariably be formed by the recurrence of the same type of stimulus which was the inciting agent in the first instance. It must be concluded, therefore, (1) that immunity is permanent, (2) that pregnancy produces an anamnestic reaction resulting in further production of antibodies or (3) that enough fetal cells escape into the maternal circulation in all pregnancies to stimulate the production of antibodies in a mother previously immunized but insufficient in most instances to initiate the process.

10. Fetuses with Rh-negative blood escape the disease. There are 5 reports in the literature describing pairs of fraternal twins in which an infant with Rh-positive blood suffered from erythroblastosis but the one with Rh-negative blood was normal.¹⁰⁰ It is known that occasionally a child escapes whose siblings have had the disease, and although there are few reports to confirm this it is probable that these infants have Rh-negative blood. Potter⁹² recently observed the first normal child in a fairly large series of infants born to mothers who had borne an infant with erythroblastosis. The mother of this child had had 3 normal children by one husband and 1 normal child by a second husband. The fifth pregnancy ended in the delivery of a hydropic fetus with typical erythroblastosis. The mother's blood was Rh negative and had a high titer of anti-Rh agglutinins six weeks after the fifth

98. (a) Potter, Davidsohn and Crunden.^{96a} (b) Hertzog, A. J.: Problems Encountered in Explaining Certain Cases of Erythroblastosis Fetalis on the Rh Theory, *Minnesota Med.* **26**:1057, 1943.

99. Levine, P.: Iso-Immunization in Pregnancy and the Pathogenesis of Erythroblastosis Fetalis, in Karsner, H. T., and Hooker, S. B.: *The 1941 Year Book of Pathology and Immunology*, Chicago, Year Book Publishers, Inc., 1941, p. 505.

100. (a) Kariher.⁴⁴ (b) Levine.⁵⁰ (c) Potter, E. L.: A Double Ova Pregnancy in Which the Rh + Twin Developed Erythroblastosis, *J. Pediat.* **24**:449, 1944.

delivery. The sixth child has been entirely well since birth and is still normal at 10 months of age. The blood of the mother six months after the sixth delivery had a high titer of anti-Rh agglutinins. The infant's blood is Rh negative. The husband's blood is Rh positive, but it is also positive to Diamond's St serum (see subsequent discussion) indicating that he is heterozygous (Rhrh). These cases give further proof that the fetus of a mother who has once become immunized must have Rh-positive blood to acquire erythroblastosis and that a fetus with Rh-negative blood will escape the disease even though exposed to an environment favorable for its development.

Further proof would exist if after having had one or more infants with erythroblastosis a woman could deliver a normal child following impregnation with Rh— sperm.

11. The administration of Rh-positive blood to a woman whose blood is Rh negative may produce sufficient immunization to cause erythroblastosis in a subsequent fetus. In the majority of instances in which a woman has had an infant with erythroblastosis in a first pregnancy a history of one or more previous transfusions can be obtained. A few women with Rh-negative blood who have given birth to several normal children and have subsequently been given a transfusion with Rh-positive blood without ill effect have in the next pregnancy delivered an infant with erythroblastosis.¹⁰¹ If these patients had been immunized against the Rh factor by the previous pregnancies, a reaction to the first transfusion of Rh-positive blood should have occurred.

12. The transfusion of Rh-positive blood into a woman whose blood is Rh-negative and who is the mother of a baby with erythroblastosis may cause a hemolytic reaction, even though the blood given appears compatible by all known tests. Anti-Rh agglutinating cannot be demonstrated in the blood of many women who have given birth to infants with erythroblastosis. The "biologic test" recommended by Wiener, Silverman and Aronson¹⁰² may give evidence of the presence of active antibodies, even though they are not demonstrable in vitro. In a typical instance⁹² a patient who had previously had 3 normal children gave birth at term to a slightly macerated fetus with erythroblastosis. The mother's blood was O Rh negative and contained no

demonstrable anti-Rh agglutinins. The husband's blood was A Rh positive. Eight days after delivery the patient was given 50 cc. of O Rh-positive blood which was compatible on cross matching by the incubation-centrifugation method. She had no reaction, and the icteric index had only risen from 6.3 to 8.1 an hour after the transfusion. At this time 50 cc. more of the same blood was injected. A severe chill followed immediately; the temperature rose to 40.2 C. (104 F.), and at the end of the second hour the icteric index was 13.2. The temperature had returned to normal three hours later. The patient had been previously alkalized, and there was no reduction in urinary output. Blood drawn two days after the biologic test still failed to show anti-Rh agglutinins. This case, as well as others which have been reported, gives evidence that immunization to the Rh factor may exist although laboratory methods used at present cannot demonstrate the existence of agglutinins.

EVIDENCE FAILING TO SUPPORT THE CONTENTION THAT ERYTHROBLASTOSIS IS AN RH ANTIGEN-ANTIBODY REACTION

1. Only a small percentage of women with Rh-negative blood give birth to infants with erythroblastosis. In approximately 9 per cent of all births an infant with Rh-positive blood is delivered by a mother with Rh-negative blood. Since the incidence of erythroblastotic infants seems to be approximately 1 to 400 births, the disease develops in only about 1 of 40 infants for whom the possibility of its occurrence exists. This low incidence is due to several factors: A. Erythroblastosis almost never occurs in a first pregnancy; thus women bearing only 1 child will have no infant with this disease. B. The total parity of the majority of women is low. The more pregnancies to which a woman with Rh-negative blood is subjected, the greater the likelihood that she will have a child with erythroblastosis. C. Since not all women with Rh-negative blood have infants with erythroblastosis in even a second or a subsequent pregnancy, it is necessary to postulate (a) that some Rh-positive fetal cells are not antigenic, (b) that in some instances the maternal organism is incapable of responding to the Rh-positive antigen, (c) that only in some pregnancies does the antigen enter the maternal circulation or (d) that some fetuses are not affected by anti-Rh agglutinins. Each of these factors doubtless operates in some instances, but the third, in view of present knowledge, seems the most important. It is probable that in the majority of women the placental vessels remain intact and no fetal cells gain entrance to the maternal circulation. Only

101. (a) Diamond.⁴⁶ (b) Potter, E.: Unpublished data.

102. Wiener, A. S.; Silverman, I. J., and Aronson, W.: Hemolytic Transfusion Reactions: II. Prevention with Special Reference to a New Biological Test, *Am. J. Clin. Path.* 12:241, 1942

when a pathologic state permits escape of fetal cells is immunization produced and the way prepared for the subsequent development of erythroblastosis.

2. The titer of maternal anti-Rh agglutinins is not proportionate to the severity of the fetal disease. There seems to be no relationship between (a) the severity of erythroblastosis in the fetus or (b) the number of affected infants to which a mother has given birth and (a) the presence of agglutinins in the maternal circulation, (b) the concentration they attain or (c) the length of time they persist. It is frequently impossible to demonstrate agglutinins in the blood of women whose infants are affected with the most severe form of the disease, while they may be present in high titer in the blood of women whose infants are only mildly affected. Dockeray and Sacks¹⁰³ recently reported testing 61 unselected pregnant women and finding 3 with irregular isoagglutinins of which at least 1 was anti-Rh. All of the women had normal infants. Dockeray and Sacks suggest that the incidence of anti-Rh agglutinins may be much higher than is supposed and postulate that some specific conditions favoring the admission of antibodies to the fetus must be present before erythroblastosis develops. Mollison¹⁰⁴ also reported that weak anti-Rh agglutinins were present during pregnancy in the blood of a woman who gave birth to a normal child with Rh-positive blood. The reason for the lack of correlation between the severity of the disease in the fetus and the concentration of antibodies in the mother's blood is unknown.

3. Some women whose blood is Rh positive give birth to infants stated to have erythroblastosis. The possible reasons for this apparent discrepancy include (1) errors in performing the Rh tests, (2) errors in making the diagnosis of erythroblastosis, (3) initiation of erythroblastosis by some other agglutinin, (4) initiation of erythroblastosis by some entirely unrelated agent and (5) immunization by a factor in one of the Rh subgroups. It is believed¹⁰⁵ that the first two possibilities function more commonly than the others. There are few published descriptions of infants with conditions diagnosed as erythroblastosis whose mothers had Rh-positive blood, but in those cases for which records

are available at least some of the diagnoses seem open to question. In the large series of reports of cases published by Levine, Katzin, Vogel and Burnham¹⁰⁶ the diagnoses were made by scores of physicians, and there is a great chance that errors have been made. The conclusion that the Rh factor has no relation to erythroblastosis which was reached by Gallagher, Danis and Jones¹⁰⁷ because the mothers of a small group of jaundiced infants had Rh-positive blood is unwarranted and seems to have been based on a misconception of erythroblastosis.

However, it appears that in rare instances maternal immunization to other antigens may occur and may produce erythroblastosis. There are a few cases in which the mother seems to have had an increase in α or β agglutinins as a result of a pregnancy in which the fetus possessed an A or B antigen that the mother's blood lacked. Boorman, Dodd and Mollison⁹⁸ reported titers of 1:3,200 and 1:8,000,000 for anti-B agglutinins in 2 mothers with Rh-positive blood who gave birth to infants with erythroblastosis. They stated that they had observed a titer as high as that shown by the first of these patients in the blood of women delivering normal children. La Vake¹⁰⁸ described a patient who belonged to group O (Rh +) who gave birth to an infant in group B who had erythroblastosis. Five weeks after the delivery the maternal titer of B agglutinins was 1:1,600. By the end of eight months it had fallen to 1:500. The early higher titer was believed due to stimulation by the B agglutinin in the cells of the fetus. If a positive diagnosis of erythroblastosis can be made in these cases and the possibility of immunization to any other antigen definitely excluded, an injury from α or β agglutinins may be presumed.

At least 5 women with infants who had erythroblastosis have been observed whose blood has contained agglutinins different from anti-Rh or any of its previously recognized variants. The first of the serums was mentioned by Levine, Katzin, Vogel and Burnham¹⁰⁶ and by Javert.¹⁰⁹ This serum, which was designated Hr, agglutinated the cells of about 50 per cent of all bloods

106. Levine, P.; Katzin, E. M.; Vogel, P., and Burnham, L.: The Antigenicity of the Rh Blood Factor in Transfusion and Pregnancy: Its Role in the Etiology of Erythroblastosis, in Mudd, S., and Thalheimer, W.: Blood Substitutes and Blood Transfusions, Springfield, Ill., Charles C Thomas, Publisher, 1942.

107. Gallagher, F. W.; Danis, P. G., and Jones, L. R.: The Rh Factor in Relation to Jaundice of the Newborn Infant, *J. Pediat.* **22**:171, 1943.

108. LaVake, R. T.: The Cause of Toxemias of Pregnancy, *Journal-Lancet* **63**:51, 1943.

109. Javert, C. T.: Further Studies on Erythroblastosis Neonatorum of Obstetric Significance, *Am. J. Obst. & Gynec.* **43**:921, 1942.

103. Dockeray, G. C., and Sacks, H.: Rh Antibodies in the Maternal Circulation Without Clinical Manifestations of Erythroblastosis in the Child, *J. Immunol.* **48**:241, 1944.

104. Mollison, P. L.: The Application of Present Knowledge About the Rh Factor, *Post-Grad. M. J.* **20**:17, 1944.

105. Potter, E. L.: The Rh Factor in Obstetrics, *M. Clin. North America* **28**:254, 1944.

and reacted especially with those which were Rh negative or contained the Rh₂ factor. The St serum of Race and Taylor⁷⁹ agglutinated all but 20 per cent of bloods and seemed to act on all cells except those of persons whose genotype was Rh₁Rh₁. Loutit⁸¹ has suggested that Rh₂, Rh₀ (Rh of Wiener, table 5) and Rh'', all of which are agglutinated by anti-St serum, may have in common a partial antigen which is responsible for the reaction to anti-St agglutinins. To which Rh subgroup the patients whose blood contained Hr or St agglutinins belonged has not been reported. It seems apparent, however, that rh, Rh₂, Rh₀ and Rh'' are all lacking in the patients whose blood contained anti-St agglutinins and that one or a combination of these factors, present in the blood of husband and of the fetus, produced the immunization. A serum believed identical to the St serum has been observed by Diamond^{47b} and by Potter and Davidsohn.⁵⁶ Levine¹¹⁰ also recently reported an additional patient whose blood contained anti-Hr agglutinins.

From a study of these rare agglutinins, as well as from the determination of the Rh subgroups which are represented by the parents of infants with erythroblastosis, it seems evident that persons may become immunized to one Rh factor even though possessing another Rh factor in his or her cells. For example, a person whose blood cells contain the factor Rh₂ may become immunized to Rh₁, Rh', or Rh₀. Although immunization of a person whose blood is Rh negative occurs much more commonly, the response of a person with Rh-positive blood to some Rh factor other than the one present in her own cells may, at times, cause erythroblastosis and is partially responsible for the erythroblastosis in the offspring of women whose blood is Rh negative.

4. The disease frequently becomes more severe immediately after birth than it was during fetal life. If erythroblastosis is caused by the transmission of anti-Rh agglutinins from the mother to the fetus, symptoms would be expected to reach a maximum during intrauterine life and to regress immediately after birth. Anemia, icterus and all signs of hemolysis, however, nearly always become progressively more intense during the first few days of extrauterine existence. A definite explanation of this has not been provided, but there is a strong suggestion in the better survival of transfused Rh-negative blood that agglutinins are still present in the blood of the infant for some time after it is born. On the other hand, almost all infants show destruc-

tion of a certain portion of the red cells during the first few days of life, and it is possible that the postnatal destruction observed in erythroblastosis is an abnormal exaggeration of this apparently physiologic process (due to an unknown cause) and not specifically related to hemolysis of cells by anti-Rh agglutinins.

5. α and β agglutinins in the maternal blood rarely, if ever, cause fetal erythroblastosis. The question is constantly raised as to why maternal agglutinins which are formed in response to the introduction of the Rh antigen should be capable of passing through the placenta and exerting a harmful influence on the fetal blood cells while α and β agglutinins entering the fetal circulation have no effect. Levine¹¹¹ has stated repeatedly that he believes this is because A and B substances are present in the tissues and fluids of the body and are therefore capable of absorbing the agglutinins and protecting the blood cells, whereas the Rh antigen is absent from the tissues and the Rh agglutinins consequently can act directly on the blood cells. He also explains the few cases of erythroblastosis in which the mother has Rh-positive blood but is of a different blood group from her husband on the basis that the child is probably a "nonsecretor"¹¹² and therefore has no A or B antigen anywhere in the body except in the erythrocytes. Although this makes an attractive theory, it appears to be based on two incompletely proved premises. Boorman and Dodd⁸⁷ have pointed out that the assumption that occasionally fetal erythroblastosis or some other fatal disease might develop from the effect of α or β agglutinins because an infant was a "nonsecretor" may be erroneous. They call attention to the fact that even in the 20 per cent of persons who fail to secrete A or B substances in the saliva, semen or other body fluids the antigen can still be obtained by alcoholic extraction of tissues, thus indicating its presence in various organs, in spite of the absence from aqueous solutions. In the second place, they have also shown that the Rh substance is present in the tissues of the body, in spite of the fact that Levine^{39b} and Wiener^{36a} assumed it absent because it could not be demonstrated in saliva or seminal fluid.

Although it may be possible that fluid antigen is more potent than tissue antigen in its ability to protect erythrocytes from being destroyed,

110. Levine, P.: Mechanism of the Isoimmunization by the Rh Factor of Red Blood Cells: Standardization of Anti-Rh Serums, *Arch. Path.* **37**:33 (Feb.) 1944.

111. (a) Levine.⁹⁴ (b) Levine, P.: Genetic and Constitutional Causes of Fetal Death, *Collecting Net*, 1942, no. 5, p. 17. (c) Levine, P.: Erythroblastosis Fetalis and Other Manifestations of Isoimmunization, *West. J. Surg.* **50**:468, 1942.

112. Schiff, F., and Sasaki, H.: Ueber die Vererbung des serologischen Ausscheidungstypus, *Ztschr. f. Immunitätsforsch. u. exper. Therap.* **77**:129, 1932.

there does not seem to be at the present time an entirely adequate explanation of why Rh agglutinins, which are frequently nondemonstrable in maternal blood, should have such a deleterious effect on the fetal cells, while α or β agglutinins, which are commonly present, should have no effect. This fact and the fact that erythroblastosis may progress for several weeks after birth form the principal difficulties in the complete acceptance of the theory that immunization to the Rh factor is the sole cause of the disease.

Prevention of Erythroblastosis.—With the fundamental causation of erythroblastosis fairly well established on the basis of maternal immunization, hope is not unwarranted that a method of maternal desensitization may be discovered. This would be of particular value in preventing a repetition of the disease. In most instances the first appearance, even with a method of desensitization, could not be prevented, since the blood of many of the pregnant women does not have demonstrable anti-Rh agglutinins and fetal erythroblastosis (by any means available at present) could not be suspected until after the baby was delivered.

Burnham¹¹³ has suggested giving large amounts of vitamin C to women who have delivered infants with erythroblastosis in the belief that vascular injury (with resultant fetal erythroblastosis) can be expected more commonly in patients with deficiency of vitamin C than in those experiencing no lack. If vitamin C is to be of value, however, it will probably have to be given during the pregnancy prior to the one in which erythroblastosis is first diagnosed. After the disease has developed in one infant, there is little reason to expect that it can be prevented in future pregnancies by the administration of vitamin C. Willson and Potter¹¹⁴ gave 200 mg. of ascorbic acid and the juice of 3 lemons daily to 2 women during the last five months of pregnancy. Both delivered babies with erythroblastosis, as they had done in previous pregnancies.

Insemination with known Rh-negative sperm from a donor should be one method of permitting a woman with Rh-negative blood to have a normal child. Since both the ova and the sperm are normal in parents with infants suffering from erythroblastosis, each person should be able to have normal children with an appropriate mate. No results of artificial insemination have been reported so far, but Potter and Willson¹¹⁴ have

recently been successful in impregnating a patient with Rh-negative sperm. The outcome of the pregnancy will be watched with much interest, and it is anticipated that a normal child will result. Changing from one mate of the Rh + phenotype to another is of no benefit. Potter⁹² has observed 5 women each of whom has had infants with erythroblastosis by 2 husbands. The 3 second husbands who were tested had Rh-positive blood.

The artificial termination of pregnancy by cesarean section as soon as the fetus becomes viable has been recommended, on the assumption that if the fetus can be delivered early enough in the course of pregnancy it may escape being affected by maternal agglutinins.¹¹⁵ It has also been suggested that the mother's blood be watched closely for the appearance of agglutinins or for a rise in agglutinin titer and that the pregnancy be terminated at the time when agglutinins appear or when the titer suddenly rises.¹⁰⁸ The statement of Rothman and Hopkins¹¹⁶ that an infant should be delivered by cesarean section with local anesthesia whenever a diagnosis of erythroblastosis has been made on a previous sibling because asphyxia is less apt to occur with abdominal than with vaginal delivery seems open to definite question. Fallon¹¹⁷ (who stated the conviction that erythroblastosis is due to infection¹¹⁸) suggested delivery by cesarean section two to three weeks prior to the expected date of confinement on the assumption that the entrance of bacteria into the fetus from an abnormally permeable placenta during labor could be prevented by abdominal delivery.

If there were no hazard associated with prematurity, early delivery might be an advisable procedure on the supposition that the more prolonged the exposure to anti-Rh agglutinins, the more severe the disease might be. It must be remembered, however, that the fetus is probably affected from early in pregnancy regardless of whether demonstrable agglutinins are present in the maternal circulation and that many infants become much more severely affected immediately after delivery than they were during intrauterine life. Too few cases have as yet been reported to indicate whether early delivery with the con-

115. Reid, D. E.: *Obstetrics: Medical Aspects*, New England J. Med. **228**:97, 1943.

116. Rothman, P. E., and Hopkins, H.: *The Relationship of Erythroblastosis Fetalis to Intrauterine Asphyxia*, Am. J. Obst. & Gynec. **45**:291, 1943.

117. Fallon, M.: *Jaundice and Conditions Associated with the Phenomenon*, J. Pediat. **23**:721, 1943.

118. Fallon, M.: *Classification of the Anemias, Blood Pictures in the Anemias and Anemias in Infants and Children in Downey, H.: Handbook of Hematology*, New York, Paul B. Hoeber, Inc., 1938, vol. 3.

113. Burnham, L.: *Vitamin C Deficiency as a Possible Factor in the Pathogenesis of Erythroblastosis Fetalis*, Am. J. Obst. & Gynec. **44**:920, 1942.

114. Willson, J. R., and Potter, E. L.: Unpublished data.

sequent discontinuation of direct exposure to anti-Rh agglutinins can outweigh the handicap of prematurity imposed on an infant already suffering from erythroblastosis. Although it is possible that under such circumstances the disease might be of a milder nature, there is no reason to believe that a fetus could be delivered sufficiently early to escape erythroblastosis. At the Chicago Lying-in Hospital, as well as in other clinics, infants have been delivered early by cesarean section only to die subsequently of erythroblastosis despite the administration of blood after birth, and it has been concluded that nothing is to be gained by premature delivery.

Treatment of Erythroblastosis.—There is no known form of intrauterine therapy for fetuses suffering from erythroblastosis which in any way will affect the course of the disease. Prior to the discovery of the cause of the condition various procedures had been recommended, almost all directed toward improving the erythrocytic state of the mother or toward stimulating erythropoiesis in the fetus by maternal administration of iron compounds, liver or vitamins. None of these substances appear to have any effect on the fetus.

After birth, the treatment of choice consists of giving the infant transfusions of Rh-negative blood of the appropriate group. Despite the fact that the infant's blood is Rh-positive, Rh-negative blood appears preferable for transfusion.¹¹⁹ Almost all infants with erythroblastosis show some progression of symptoms after birth, which indicates a continuing exaggerated destruction of erythrocytes after exposure to the intrauterine environment has ceased. If Rh-negative erythrocytes are added to the circulating blood, they should escape destruction, since they contain no antigen to be affected by anti-Rh agglutinins. The total volume of blood in the average newborn infant is between 250^{119e} and 350 cc.¹²⁰; therefore, if all of the infant's Rh-positive cells were destroyed it would be possible to replace them with Rh-negative cells by transfusion. Tests of differential agglutination have

shown rapid destruction of transfused Rh-positive cells and the normal survival of Rh-negative cells in several infants.⁸⁹

If Rh-negative blood cannot be obtained except from the mother, Wiener and Wexler^{119e} have suggested the use of maternal cells which have been washed and suspended in isotonic solution of sodium chloride or normal blood plasma. They further suggested that this might be the method of choice on all occasions, inasmuch as in rare instances it is possible for some factor other than Rh to be responsible for the production of erythroblastosis, and whatever the antigen in the infant responsible for the disease, it would be absent in the mother. If maternal blood cells (washed free of antibodies) were given the baby they would be completely resistant to destruction by antibodies which might have been transmitted to the fetus in utero. It has been shown that agglutinins against the mother's cells are never present in the infant at birth and that consequently maternal cells can be safely given an infant during the first few days of life regardless of differences in blood group.¹²¹

The administration of Rh-positive blood is preferable to giving no blood at all. In infants with profound anemia an immediate transfusion may be a life-saving measure. Intramuscular or intraperitoneal injection of blood is of practically no value and should not be used.

The time at which to give a transfusion and the amount of blood to be given must be settled for each individual case. An infant with erythroblastosis who has less than 3,000,000 erythrocytes per cubic millimeter of blood at birth should ordinarily be given a transfusion as soon as possible. If the count is below 2,000,000, a delay of a few hours may be fatal. Many infants with counts as low as this at birth will die, regardless of treatment. Irreparable damage (probably from chronic anoxia) seems to have been produced in utero and cannot be cured by the administration of any amount of blood after birth.

Gimson^{95b} gave an erythrocyte count of 3,500,000 as a level below which all infants with erythroblastosis should be given transfusions. With counts higher than this immediate transfusion is ordinarily not necessary and frequently not even to be desired. For the first few days determinations of the number of erythrocytes should be repeated at intervals of approximately twelve hours and a transfusion should be given immediately if evidence of a rapid decrease occurs. Even with a gradual decrease the count

119. (a) Levine, Burnham, Katzin and Vogel.^{31b} (b) Boorman, Dodd and Mollison.^{47a} (c) Mollison.⁸⁹ (d) Gimson.^{95b} (e) Rh in Prognosis and Treatment of the Hemolytic Disease of the Newborn, editorial, Brit. M. J. 1:303, 1943. (f) Wiener, A. S., and Wexler, I. B.: Transfusion Therapy of Acute Hemolytic Anemia of the Newborn, Am. J. Clin. Path. 13:393, 1943. (g) Brown, H. R., and Levine, P.: The Rh Factor and Its Importance in Transfusion for the Anemias of Erythroblastosis and Other Causes, J. Pediat. 23:290, 1943.

120. DeMarsh, Q. B.; Winkle, W. F., and Alt, H. L.: Blood Volume of the Newborn Infant in Relation to Early and Late Clamping of the Umbilical Cord, Am. J. Dis. Child. 63:1123 (June) 1942.

121. Polayes, S. H.; Lederer, M., and Wiener, A. S.: Studies in Isohemagglutination: The Landsteiner Blood Groups in Mothers and Infants, J. Immunol. 17:545, 1929.

should probably not be allowed to go much below 3,000,000 before transfusions are given.

English investigators have reported salutary effects from the administration by the drip method over a period of several hours of 120 to 150 cc. of blood. One or at most two transfusions of this amount of Rh-negative blood are ordinarily sufficient.

Most American investigators appear to prefer giving smaller amounts of blood by direct injection and rarely give more than 10 cc. per pound (20 to 22 cc. per kilogram) of body weight at one time. If the cells administered are not destroyed, three or four transfusions of this size should be sufficient for the alleviation of even the most severe conditions.

The normal period of survival of transfused cells appears to be about eighty to one hundred and twenty days.⁹⁷ By the end of this time all effect of maternal agglutinins should have been lost and the infant should be manufacturing its own cells. When transfusions do not give the expected increase in circulating erythrocytes, as frequently happens when Rh-positive blood is used, there is often a tendency to give more and more blood. A resultant increase in hemolysis leads to constantly increasing amounts of bilirubin in the blood, and the extremely high levels which may be produced greatly increase the danger of damage to the brain (kernicterus).

Methods of therapy other than transfusion probably have little effect early in the course of the disease; after the infant has survived the first few days of life, administration of iron compounds or liver may help in speeding up the process of complete recovery.

The administration of vitamin K has been suggested¹²² as a means of combating the hemorrhagic tendency that is occasionally present. Its use is probably to be recommended, although in most cases hemorrhage appears to be due to hepatic damage and not to a direct lack of vitamin K. The administration of vitamin K frequently fails to prevent hemorrhage.

The addition to the diet of dextrose and preparations containing choline in an attempt to combat the ill effects of possible hepatic damage has been recommended by Danis and Anderson.¹²³ McKinley¹²⁴ attributed a decrease in

mortality in infants with erythroblastosis to the administration of calcium gluconate and extract of liver, the latter given intramuscularly.

Splenectomy¹²⁵ had been advocated as a method of treatment prior to the discovery of the cause of erythroblastosis. In view of the causation this form of therapy seems to have no justification.

RELATIONSHIP OF THE RH FACTOR TO OTHER CAUSES OF FETAL AND NEONATAL MORTALITY

Levine¹²⁶ postulated maternal immunization to the Rh factor as influential in abortions, malformations and other causes of fetal deaths. The assumption that it might be related to the production of malformations appears to have been based on two studies which indicated that an abnormally high incidence of malformations exists in infants with erythroblastosis.¹²⁷ Potter,⁹² however, has observed no malformation in over 100 infants and fetuses with erythroblastosis. The mothers of 67 infants and fetuses dying of miscellaneous causes, including malformations, showed only a slightly higher incidence of Rh-negative blood than is found in the general population.⁹⁶

Although women bearing infants with erythroblastosis have a high incidence of abortions, it does not follow that abortions are frequently due to immunization to the Rh factor. Even Levine⁹³ seems to have concluded that there is probably little relation between the majority of early abortions and the Rh factor. In place of this, however, he has stressed the importance of heterospecific pregnancy—a pregnancy in which the fetus possesses an A or B antigen which is lacking in the mother—and has stated that fetal death is probably due to a reaction between the A or B antigen normal to the fetus and the α or β agglutinin transmitted from the mother. He has attempted to show^{126c} a higher than normal incidence of heterospecific pregnancies in pregnancies ending in abortion or fetal death of unknown cause and a lower than normal incidence of offspring in group A when the mother is of group O and the father of group A than when the mother is of group A and father of group O.

To date there has been no satisfactory proof that the Rh factor is responsible for any condition other than erythroblastosis or that α or β

122. Mayman, E. W.: Erythroblastosis in Icterus Gravis Neonatorum Successfully Treated with Vitamin K, *J. Pediat.* **17**:806, 1940.

123. (a) Danis, P. G.: The Pathogenesis of Jaundice in the Newborn Infant, *J. Missouri M. A.* **40**:62, 1943. (b) Danis, P. G., and Anderson, W. A. D.: Choline Chloride in the Treatment of Icterus Gravis Neonatorum, *South. M. J.* **35**:1070, 1942.

124. McKinley, H.: Icterus Gravis Neonatorum with Erythroblastosis, *Arch. Dis. Childhood* **16**:63, 1941.

125. Hardwick, C., and Lloyd, O.: Icterus Gravis Cured by Splenectomy, *Lancet* **2**:339, 1941.

126. (a) Levine.^{111b} (b) Levine.^{111c} (c) Levine, P.: Serological Factors as Possible Causes in Spontaneous Abortion, *J. Hered.* **37**:71, 1943.

127. (a) Hawksley and Lightwood.^{82b} (b) Javert.¹⁰⁹

agglutinins transmitted to the fetus harm it in any way.

RELATIONSHIP OF THE RH FACTOR TO REACTIONS TO TRANSFUSIONS

Little more needs to be added about the importance of the Rh factor in relation to the cause and prevention of reactions to transfusions. Immunization to the Rh factor has been shown to be the cause of reactions in approximately 60 persons since its discovery¹²⁸ (table 7). From the present concept of the Rh antigen it would appear that under ideal conditions each person prior to receiving a transfusion should have his

TABLE 7.—*Hemolytic Reactions to Transfusions Due to the Presence of Anti-Rh Agglutinins*

	Patients Having Infants with Erythroblastosis		No Erythroblastosis in Offspring or Date Lacking			
	Total Num-ber	Agglu- tinins in Died Blood	Fe- male		Agglu- tinins in Male Died Blood	
Wiener and Peters ²⁸	2	1	1	3
Wiener ²⁸	7	5	2	3
Wiener and Forer ^{30a}	1	1
Wiener et al. ¹⁰²	1	1
Wiener *.....	2	2
Levine et al. ³⁰	3	2	3	1	1	1
Levine et al. ¹⁰⁰	3(?)	3
Levine ^{111c}	5	3	5
Schwartz and Levine ⁹⁵	1
Brown and Levine ^{119f}	1
Dameshek and Levine ^{128c}	1	1
Vogel et al. ⁴⁹	4	5	..	5
Mayer and Vogel ^{128d}	1	1
Scott and Conant ²⁹	1	..	1	1
Koucky ⁸⁹	1	..	6	4
Mollison ^{43b}	1	..	1	1
Mollison ⁸⁹	2	..	2
Boorman et al. ^{47a}	2	1	..	3
Newton and Tebbutt ⁵²	1	1
Diamond ⁴⁶	5	..	5	1	..	3
Karlher and Spindler ^{83c}	1	..	1
Aagaard ^{128a}	2	..	2
Crooks ^{128b}	1	1
Poncher et al. ^{128e}	1	1
Adam ^{140a}	1
Total.....	19	5	19	41	11	36

* Personal communication.

Rh status determined. If a person has Rh-positive blood, any blood of the appropriate AB group should be tolerated. If the blood of the patient is Rh negative it would seem best to use Rh-negative blood for transfusion if possible. Any person, man or woman, with Rh-negative blood must be considered as potentially capable

128. (a) Aagaard, G. N.: Transfusion Reactions and Erythroblastosis Foetalis Caused by the Rh Factor, *Minnesota Med.* **25**:267, 1942. (b) Crooks, P. E.: Blood Transfusion Reaction Due to Intragroup Incompatibility, *Am. J. Obst. & Gynec.* **44**:121, 1942. (c) Dameshek, W., and Levine, P.: Isoimmunization with the Rh Factor in Acquired Hemolytic Anemia, *New England J. Med.* **228**:641, 1943. (d) Mayer, M. D., and Vogel, P.: Intra-group Hemolytic Transfusion Reaction Due to the Rh Agglutinin as a Result of the Isoimmunization in Pregnancy, *J. Mt. Sinai Hosp.* **8**:300, 1941. (e) Poncher, H. G.; Weir, H. F., and Davidsohn, I.: Observations on Hemolysin in Acute Hemolytic Anemia, *J. Pediat.* **52**:387, 1943.

of becoming immunized to Rh-positive blood. If a single transfusion is given to a man, determination of the Rh factor is unnecessary. It is impossible, however, to be certain that there will never be subsequent need of more blood, and it seems possible that on rare occasions one or two transfusions may produce sufficient immunity to be the cause of a hemolytic reaction many years later. Theoretically no girl or woman with Rh-negative blood should be given Rh-positive cells from birth to the end of reproductive life because of the possibility that they might cause an immunity which would produce erythroblastosis in infants born later.

A large proportion of women with Rh-negative blood who have been pregnant have had a chance to develop anti-Rh agglutinins, and it is extremely important that such women should be given Rh-negative blood. Most important of all is the use of Rh-negative blood for any woman with Rh-negative blood who has given birth to an infant with erythroblastosis. In such cases it is frequently imperative.

If it is impossible to determine whether the blood of the patient or of the donor is Rh negative, careful cross matching by the incubation-centrifugation technic followed by the use of Wiener's "biologic test" is essential if blood must be given to a woman who has had an infant with erythroblastosis.

Of increasing importance is the determination of the Rh status and the giving of Rh-negative blood by transfusion to persons with Rh-negative blood if the patient is (1) a boy or man apparently in need of a single transfusion, (2) a boy or man apparently in need of multiple transfusions, (3) a girl or woman who has never been pregnant, (4) a woman who has been pregnant but has had no abortions or stillbirths and has lost no infant by neonatal death, (5) a woman who has had an abortion or a stillbirth or who has lost an infant by a neonatal death not diagnosed as due to erythroblastosis, (6) a woman who has given birth to an infant with erythroblastosis but whose blood shows no anti-Rh agglutinins, (7) a woman who has had an infant with erythroblastosis and whose blood shows anti-Rh agglutinins or a man whose blood contains agglutinins as a result of previous transfusions. Persons in group 6 should never under any circumstances be given Rh-positive blood and those in group 5 should not receive it if it can possibly be avoided.

LABORATORY TESTS FOR RH AGGLUTINOGEN AND AGGLUTININ

Testing for the Rh Factor.—Two methods for the determination of the presence or absence

of the Rh factor have been described. The choice of method depends largely on whether the source of the testing serum is animal or human, although the two methods may be used interchangeably or combined. Since agglutination is rarely intense, the slide technic such as that frequently used for AB grouping is not ordinarily satisfactory. Tests for the Rh factor are more difficult than those for A and B substances, and the performance and interpretation require more experience.¹²⁹

HUMAN SERUM: One to two drops of a 2 per cent suspension of the red blood cells in isotonic solution of sodium chloride is placed in a test tube of 7 mm. bore, and an equal amount of testing serum is added. The mixture is lightly shaken and placed in an incubator or waterbath at 37 C. for one hour. It is then centrifuged at 500 revolutions per minute for one minute and again lightly shaken. If agglutination is not visible to the unaided eye, the mixture in the tube is examined with a hand lens or the tube is placed on the mirror and examined under the low power of a microscope. If neither of these examinations is conclusive, a drop of the suspension is placed on a slide and examined microscopically. Care must be taken not to shake the suspension too vigorously or agglutinated cells may be separated. When reactions are weak, it may be difficult to tell whether true agglutination or rouleau formation is responsible for the appearance. The use of serum of sufficiently high titer to permit dilution reduces the likelihood of rouleau formation.^{47a}

Because of the variability in the agglutinins in different human serums it is advisable for one to perform the tests with not less than three different serums before a diagnosis is made.¹³⁰ Known Rh-positive and Rh-negative cells should be set up simultaneously with the same serums to act as controls. Clotted whole blood or concentrated citrated blood if kept in a refrigerator may be used satisfactorily for a period up to two weeks if fresh suspensions of cells are made at the time of testing.

Several investigators¹³¹ recommend washing the cells before making the suspension. The suspension should always be freshly prepared immediately before making the test. Suspensions with more than 2 per cent concentration of

blood sediment are especially apt to give false negative reactions, while those with less than 2 per cent commonly give inconclusive results.

Certain serums have been described which are more active at refrigerator or room temperature than at 37 C.²³ The majority, however, react most favorably at 37 C. and show little or no agglutination at lower temperatures. Fisk and Foord⁶⁸ stated that lower dilutions of potent serum will frequently give the same reaction at room temperature that higher dilutions will give at 37 C. The use of higher temperatures thus conserves testing material. The optimum dilution and temperature for activity for each serum should be determined prior to use, and the tests should be performed under correct conditions.¹³²

ANIMAL SERUM: One to two drops of a 2 per cent suspension of cells and 2 drops of serum are placed in a 7 mm. bore test tube, as in testing with human serum. Animal serum in general reacts as well at 20 C. as at 37 C., so the tubes may be kept at room temperature. After thirty to sixty minutes the sediment in the bottom of the tube is examined with the aid of a hand lens. Negatively reacting blood shows a compact circular sediment with a smooth edge, while positively reacting blood has a loose wrinkled sediment with a serrated border or a peripheral granular deposit.⁵⁷ After the first examination the mixture is shaken and reexamined an hour later, when the sediment has reformed. The tubes are then gently shaken and the suspension examined microscopically; the samples which react negatively are mostly homogeneous, while those which react positively show various degrees of agglutination. It is stated that at times the clumping is weak in spite of the presence of a positive pattern of sedimentation. Landsteiner and Wiener⁵⁷ commented that it may be necessary to repeat the test several times before arriving at a definite conclusion. Bloods of known negative and positive reactions should be set up with each unknown.

It would appear that the use of animal serum requires more experience and technical ability and is more susceptible to false diagnosis than the use of human serum.

The only investigators to report the satisfactory use of a slide technic are Simmons, Graydon, Jakobowicz and Bryce.¹³³ They kept mixtures of cells and serum on slides in moist chambers at 20 C. and at 37 C. and obtained agglutination of Rh-positive cells in fifteen to

129. Thalhimer, W.: Blood Typing and Criteria for Blood-Typing Serums, *J. Pediat.* **23**:715, 1943.

130. (a) Potter, Davidsohn and Crunden.^{96a} (b) Taylor, G. L.: Tests for the Rh Factor and Its Antibody, *Proc. Roy. Soc. Med.* **36**:225, 1943.

131. (a) Wiener.⁶⁰ (b) Fisk and Foord.⁶⁸ (c) McIvor, B. C., and Lucia, S. P.: Rapid Method for Obtaining Anti-Rh Serum from Guinea Pigs, *Proc. Soc. Exper. Biol. & Med.* **52**:293, 1943.

132. (a) Thalhimer.¹²⁹ (b) McIvor and Lucia.^{131c}

133. Simmons, R. T.; Graydon, J. J.; Jakobowicz, R., and Bryce, L. M.: The Rh Factor: Its Incidence in a Series of Victorian Red Cross Donors, *M. J. Australia* **2**:496, 1943.

sixty minutes. The test tube technic gave complete corroboration whenever used. Occasionally serums have been found in other laboratories which also gave rapid agglutination on slides,^{47b} but with the majority of the serums which are available it is necessary to use a more sensitive technic.

Determining the Presence of Anti-Rh Agglutinins.—Serum to be tested for the presence of anti-Rh agglutinins is used in place of known serum and the tests carried out as described for human or animal serum depending on the source of serum and the preference of the investigator. It is recommended that the serum be tested with a minimum of ten suspensions of cells, of which at least two contain known Rh-positive cells and two Rh-negative cells. If the serum agglutinates the known Rh-positive cells and the majority of the unknown cells and fails to agglutinate the known Rh-negative cells, it can be assumed that the agglutinin present is anti-Rh. Boorman, Dodd and Moliscn^{47a} have stated that it is advisable to test the serum against the patient's own cells to be certain that abnormally powerful autoagglutinins are not responsible for the clumping of cells. If autoagglutinins are present, they may be partially removed by leaving the serum in contact with its own clot at refrigerator temperature and then removing the serum while it is still cold.

If fresh serum is used, Wiener^{6c} and Taylor^{130b} have recommended its inactivation at 56 C. for ten to twenty minutes in order to destroy an inhibitory substance which is occasionally present.

Taylor and his associates¹³⁴ have shown that at times there is a noticeable zone phenomenon. Serum which completely failed to agglutinate cells when used full strength in some instances gave a strong reaction when diluted. Almost all serums examined gave stronger reactions at dilutions of 1:4 and 1:8 than in the undiluted state. Taylor and his associates recommended that all tests for the presence of anti-Rh agglutinins should be run in multiple dilutions before a decision is reached that agglutinins are absent.

Great variation in the reactivity of the red blood cells of different persons has been noted, some reacting poorly (but positively) to all serums and others giving strong agglutination with some and weak agglutination with others. Cells known to react well with most serums should be used as controls in testing for the Rh factor and for the presence of agglutinins. Wiener's work on the variety of Rh types ex-

plains much of the variation in reaction. He has shown a definite relationship between the degree of agglutination and the subgroup to which the Rh factor in the cells belongs.

When attempts are made to determine changes in the titer of anti-Rh agglutinins, care must be taken to use blood cells from the same person or cells known to be of the same Rh type for all titrations. A difference in the ability of the cells to react may otherwise give a false impression of a change in the concentration of agglutinins.

Cross matching prior to all transfusions should ideally be carried out by the method described for the determination of the Rh factor, using the patient's serum and the prospective donor's cells. Control tests should always be performed.⁸⁹ The work of Taylor and his associates indicates that cross matching should also be set up with at least four dilutions, 1:1, 1:2, 1:4 and 1:8. The test tube incubation method is especially important if the patient is known to have Rh-negative blood or has had a previous transfusion or pregnancy.

Preparation of Testing Serum for Rh Determinations.—ANIMAL SERUM: In the original discovery of the Rh factor Landsteiner and Wiener²⁵ used serum which was obtained from rabbits that had received a course of intravenous injections of blood from the Rhesus monkey. They subsequently demonstrated that guinea pigs gave a more satisfactory response than rabbits. After beginning with two injections⁸⁷ of washed cells from 2 cc. of blood at five day intervals, they finally increased the number of injections to five,¹³⁵ using the same amount of blood each time. The animals were bled one week after the last injection, and satisfactory serums were pooled.

Although various minor modifications have been suggested by other investigators, no entirely satisfactory method of producing animal serum has yet been devised. Guinea pigs react somewhat more favorably than rabbits, but it is rare to get a serum which is satisfactory from more than half of the animals given injections, and often serum from only 2 or 3 can be used.¹³⁶

The original investigators recommend that before use pooled guinea pig serum that is preserved with 1:1,000 merthiolate be inactivated

134. (a) Taylor^{130b} (b) Taylor G. L.; Race, R. R.; Prior, A. M., and Ikin, E. C.: Optimal Proportions of Antigen and Antibody in Tests for Rh Antibodies, *Brit. M. J.* 2:572, 1942.

135. Landsteiner, K., and Wiener, A. S.: Tests for the Rh Factor with Guinea Pig Immune Serum, *Proc. Soc. Exper. Biol. & Med.* 51:313, 1942.

136. (a) Hoare, E. D.: Occurrence of the Rh Antigen in the Population: Notes on Five Cases of Erythroblastosis Foetalis, *Brit. M. J.* 2:297, 1943. (b) Dahr, P.: Die bisherigen Untersuchungen ueber die Vererbung der neuen agglutinablen Blutkörpereigenschaft "Rh," abstracted, *Bull. War Med.* 3:448, 1943.

at 56 C. for one hour and serum that is fresh be diluted ten times with isotonic solution of sodium chloride and adsorbed for one hour at room temperature with one-tenth volume of washed blood sediment containing equal parts of A₁ and B blood. It is stated to make no difference whether the blood used for adsorption is Rh positive or Rh negative. Further dilution of the adsorbed serum to 1:4 at the time of use seems to enhance its ability to differentiate Rh-positive from Rh-negative cells.

Gallagher and Jones¹³⁷ prepared guinea pig serum for use by diluting one volume of serum with three volumes of isotonic solution of sodium chloride and adding one volume of packed, washed M Rh-negative erythrocytes of any group with respect to factors A and B. They found that if the serum was not inactivated prior to use the cells tested were apt to become hemolyzed instead of agglutinated. They¹³⁷ also reported the successful production of anti-Rh serum by the injection of human cells instead of monkey cells into guinea pigs. Various doses of O MN Rh-positive cells were given during a period of three months. The serum after adsorption with O MN Rh-negative cells differentiated sharply between human Rh-positive and Rh-negative cells.

Fisk and Foord⁶⁸ found that guinea pig serum differentiated much more sharply, between Rh-positive and Rh-negative cells and could be used in greater dilutions if it was adsorbed once in a dilution of 1:10 with a half volume of Rh-negative washed blood sediment. A 1:20 dilution of the serum was used for the final tests.

HUMAN SERUM: When the presence of anti-Rh agglutinins of sufficiently high titer in serum from any patient has been established, the serum, after appropriate treatment, may be used as testing material. Unless the serum is obtained from a patient of group AB or used only to test persons of the same blood group, isoagglutinins must be removed by the addition of boiled saliva prepared according to the method outlined by Wiener,¹³⁸ or by the addition of Witebsky's¹³⁹

purified A and B substances. The serum should be inactivated by heating for ten to twenty minutes at 56 C. if it is used fresh. Before its suitability is established its reaction to a large number of samples of human cells, preferably at least one hundred, must be known. The serums that are most desirable agglutinate 85 per cent of all cells, and their reactions in general parallel those given by animal serum. Serums giving other percentages of positive reactions are valuable for demonstrating the presence of variants of the Rh antigen. Several different serums should be used whenever cells are to be tested; at least one should give positive reactions with 85 per cent of unselected samples tested.

The majority of women whose blood contains agglutinins have an antibody titer so low that the serum cannot be used for testing. It is estimated that suitable serum can be obtained from only about 1 of 4,000 pregnant women. A method has recently been developed, however, which promises to make more serum available. Although a relatively small yield is obtained, serum which previously was of no value may be converted into material valuable for testing by concentration of the antibody-bearing globulin fraction.

SUMMARY

In the short time that has elapsed since the discovery of the Rh factor and the establishment of its relation to erythroblastosis and to reactions to transfusions, information concerning it has become remarkably general. In addition to the investigative work that has been reported, numerous general reviews have been published by Levine and by other interested persons.¹⁴⁰

137. Gallagher, F. W., and Jones, L. R.: Production of Rh Antiserums by Inoculation of Guinea Pigs with Human Erythrocytes, *Proc. Soc. Exper. Biol. & Med.* **53**:119, 1943.

138. (a) Wiener and Forer.⁶⁸ (b) Wiener.⁶⁰

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(Footnote continued on next page)

There seems little doubt that in most instances the fundamental cause of erythroblastosis is the immunization of a mother with Rh-negative blood by the Rh-positive blood of the fetus. An added factor is involved, the nature of which has not yet been determined. It is generally presumed to be an abnormality in the placenta which permits the escape of fetal cells. Haldane⁷⁴ postulated that a gene causing abnormal placental permeability must be present in addition to the one determining the Rh-negative state before erythroblastosis occurs. Wiener stated that the capacity to become sensitized is constitutional¹⁰² and is on a definite genetic basis as evidenced by the inheritance of certain allergic diseases.¹⁴¹ Potter⁸² questioned over 50 women who had given birth to infants with erythroblastosis concerning the occurrence of hay fever, asthma and allergic reactions to foods, drugs or other substances and found that less than 15 per cent had any allergic manifestations. Reproductive histories of the mothers and maternal grandmothers of these 50 women, with 1 exception, failed to show any evidence that erythroblastosis might have been present in any of their children. One patient (the one with whom this particular investigation started) stated that she was the fourth child and that her mother subsequently had had 5 miscarriages. The cause given was the short interval between pregnancies. This was the only case in which there was any suggestion that mother and daughter may both have given birth

to infants with erythroblastosis. Although the majority of the mothers of infants with erythroblastosis had sisters with children there was no evidence suggesting the possibility of erythroblastosis in any of their offspring. Taylor, Campbell and McFarlane⁵¹ and others have observed that there are fewer normal siblings born after an infant with erythroblastosis than would be expected if the incidence of heterozygosity in fathers of such infants were similar to that in the general population. This has suggested that erythroblastosis is more apt to occur when the father has two Rh-positive genes than when he has only one. By the use of their St serum Taylor and Race have been able to show that this is true.¹⁴² Of 38 fathers of infants with erythroblastosis only 5 were of the genotype Rh,rh, while of 38 phenotypically Rh-positive men selected at random 15 were of the genotype Rh,rh.

Although it is impossible to say why an immunity to the Rh antigen is developed in certain women with Rh-negative blood and not in others, all of the observations which have been made by the present author and all of the data thus far published show no exception to the following facts: 1. When a patient once has an offspring with erythroblastosis caused by immunization to the Rh factor, all subsequent children are affected unless they have Rh-negative blood. 2. Fertilization by Rh-positive sperm will produce a child who will have erythroblastosis if any previous sibling has had the disease. 3. An infant with Rh-negative blood may escape the disease in an environment that produces it in a twin with Rh-positive blood. 4. There is no evidence of direct inheritance of erythroblastosis. 5. There is no maternal abnormality of any kind which is constantly associated with this condition. 6. If a woman has given birth to an infant with erythroblastosis, a hemolytic reaction will usually develop if she is given a transfusion of Rh-positive blood.

Chicago Lying-in Hospital.

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Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

ELECTRON MICROSCOPE STUDIES OF BACTERIAL VIRUSES.
S. E. LURIA, M. DELBRUCK and T. F. ANDERSON,
J. Bact. **46**:57 (July) 1943.

The electron microscope, recently introduced as a tool for biologic research, has been applied with great enthusiasm to the study of animal and plant viruses. The authors have investigated 4 strains of bacterial viruses. In all cases the particles of virus could be identified on the micrographs. Three of these strains show "sperm-shaped" particles consisting of a head and a tail. The micrographs of 2 viruses which act on the same strain of *Escherichia coli* demonstrated the adsorption of virus on the host and, after the predicted time, the lysis of the host with the liberation of virus particles of the infecting type. Along with the virus particles, the lysing cells shed protoplasmic material of uniform granular structure, and the size of these granules was much smaller than that of the particles of virus. For a discussion of the bearing of these results on the problems of the nature of viruses the original paper should be consulted.

STOESSER, Minneapolis.

SALMONELLA ENTERITIDIS: EXPERIMENTAL TRANSMISSION BY THE ROCKY MOUNTAIN WOOD TICK, *DERMACENTOR ANDERSONI* STILES. R. R. PARKER and EDWARD A. STEINHAUS, *Pub. Health Rep.* **58**:1010 (July 2) 1943.

The authors present data to show that when *Salmonella enteritidis* is ingested by the Rocky Mountain wood tick the bacterium survives in the tick and can be transmitted by it. This may occur as long as thirty-five days after a meal of infective blood. This is the second bacterium shown to be transmissible by *Dermacentor andersoni*. The first was *Pasteurella tularensis*.

SANFORD, Chicago:

Metabolism; Infant Feeding; Milk and Other Foods

FURTHER STUDIES ON THE SYMPTOMS OF MANGANESE DEFICIENCY IN THE RAT AND MOUSE. MAURICE E. SHILS and E. V. MCCOLLUM, *J. Nutrition* **26**:1 (July) 1943.

The authors present a new solid basal diet which is extremely low in manganese. Female rats started on the manganese-low diet at weaning produced non-viable young, owing to deficiency of manganese. The estrus cycle was not disturbed in the first generation of females on this deficient diet. The same results were noted in mice. Growth was not decreased in the deficient rats of the first generation on the basal diet. When the offspring, particularly the male offspring, of stock females which had been placed on the deficient diet late in pregnancy were kept on the low-manganese diet they were inferior in growth to littermates which were given manganese. An increase in the calcium and phosphorus contents of the basal diet produced a decrease in growth of first generation males. For optimum growth, manganese is essential. The deficient males were sterile. Loss of both equilibrium and coordination was noted in the young rats on the

manganese-deficient diet. A definite decrease in activity of arginase in the livers of the deficient rats was noted. The symptoms of manganese deficiency, production of inferior young, poor growth of the female and sterility and poor growth of the male could be eliminated by the addition of manganese to the diet.

FREDEEN, Kansas City, Mo.

THE AMINO ACIDS REQUIRED FOR GROWTH IN MICE AND THE AVAILABILITY OF THEIR OPTICAL ISOMERS.
CLIFFORD D. BAUER and CLARENCE P. BERG, *J. Nutrition* **26**:51 (July) 1943.

In mice fed mixtures of twenty purified amino acids as the source of protein nitrogen moderate growth was obtained. Only the natural forms of valine, leucine, isoleucine and threonine could be utilized for this purpose and both optical forms of methionine and phenylalanine. The elimination of arginine from the diet did not retard the rate of growth; apparently the mouse is able to synthesize arginine at a fairly rapid rate. When the source of protein nitrogen was limited to the seven amino acids already mentioned (valine, leucine, isoleucine, threonine, methionine, phenylalanine and arginine) plus lysine, tryptophan and histidine, slow growth occurred.

FREDEEN, Kansas City, Mo.

EFFECT OF LEAD ABSORPTION ON BLOOD CALCIUM.
WENDELL V. JENNETTE, *Pub. Health Rep.* **58**:1001 (July 2) 1943.

Investigation of the content of calcium in the blood serum of animals ingesting large amounts of lead as well as of animals receiving smaller doses over a longer period of time at different levels of intake of calcium indicates that absorption of lead does not appreciably affect the level of calcium in the blood.

SANFORD, Chicago. [AUTHOR'S SUMMARY]

REPORT ABOUT NUTRITION IN ECUADOR. CARLOS ANDRADE MARÍN, *Bol. Inst. internac. am. de protec. a la infancia* **17**:37 (July) 1943.

The author concludes that the council of the International American Institute for the Protection of Childhood might recommend to the government of Ecuador these important measures for improving the nutritional status of the people: (1) creation of a national institute of nutrition or at least appointment of a special committee as suggested in the third resolution of the eighth Pan-American Congress, and (2) changes in the policy of production and consumption of milk in order to provide pure and guaranteed milk for children.

EDITOR'S SUMMARY.

REPORT ABOUT NUTRITION IN URUGUAY. JUAN ANTONIO COLLAZO, *Bol. Inst. internac. am. de protec. a la infancia* **17**:125 (July) 1943.

The nutrition of children begins in the prenatal period, when the expectant mother should be provided with abundant nutrient elements. In Uruguay, as in nearly all the world, it is necessary to encourage greater consumption of milk, citrus fruits, fish, vegetables and meat by children of different ages. The statistics available are insufficient and incomplete, but it may be noticed that in the city and to a greater

extent in rural areas the average diet is lacking in protective agents such as vitamins, minerals and specific amino acids.

Almost all of the national wealth is dedicated to the commercial production of foods of the highest biologic value, proteins from animal source, vitamins, citrus fruit, milk and grain.

Development of the potential wealth, commercially unexploited, of the fishing grounds which are so abundant along the shores of Uruguay and scientific improvement of dairying and of the citrus industries in this period of emergency would allow increased exportation of meat. These desirable advances would require capital stock and inter-American credit.

Statistics show an apparently high consumption of "protective" and "essential" foods by the Uruguayan population as well as by the Argentine population, but it is evident that only in the cities of Montevideo and Buenos Aires is the population able to eat well; in the rest of the country the lack of protective and essential foods produces a state of nutritional deficiency, with subsequent danger to public health and detriment to the efficiency of the persons concerned.

By a wise policy for national nutrition, such as those recently planned at the National Conference on Nutrition for Defense (Washington, 1941), at the American Conference of Business and Productive Associations (Montevideo, 1941) and at the Third International Conference on Nutrition, held under the auspices of the League of Nations (Buenos Aires, 1939), the nutrition of the people of the Americas can be improved so as to change them into a healthy, prolific and brave group of people, able to be efficient at work and to defend the rights of liberty.

In Uruguay the families of moderate income could be the best fed in the world, for there is no other country so well provided with the foods specified by modern nutritional science.

EDITOR'S SUMMARY.

PRESENT CONDITION OF THE PROBLEM OF NUTRITION IN THE AMERICAN COUNTRIES: STATEMENT OF THE PROBLEM IN VENEZUELA. Bol. Inst. internac. an. de protec. a la infancia, **17**:139 (July) 1943.

In Venezuela the present deficiency in nutrition is related to the traditional habits of the people and to the low income of the working class and the rural group; both of these factors contribute to the excessive consumption of carbohydrates and to the deficiency of proteins and vitamins in the diet. To get an adequate nutritional allowance for his family the Venezuelan worker has to spend 60 to 75 per cent of his salary for food. Several studies made in Caracas have demonstrated that 78.32 per cent of the cystrophies in children are due to lack of food.

Some of the measures already adopted by the government for the betterment of the nutrition of the population are the following: (a) Distribution of free milk to children and mothers attending the clinics for the care of children; in 1941 the ministry of public health and social assistance distributed 507,350 liters of milk; (b) creation of school lunchrooms; at present there are forty of them throughout the country the average meal served provides 1,223 calories and 70 Gm. of protein, 440 mg. of calcium and 733 mg. of phosphorus, at the cost of 0.50 bolívars per capita per day; (c) establishment and support of two popular restaurants; (d) initiation of measures to insure a higher basic level of wages; (e) extensive protection of agriculture and cattle breeding; (f) enactment, in the year

1941, of the social insurance law (providing benefits for diseases and maternity), and (g) beginning of an intensive educational program.

FROM THE EDITOR'S SUMMARY.

Vitamins; Avitaminoses

EFFECTS PRODUCED BY VITAMIN D ON ENERGY, APPETITE AND OESTROUS CYCLES OF RATS KEPT ON AN EXCLUSIVE DIET OF YELLOW CORN. CURT P. RICHTER and KATHERINE K. RICE, Am. J. Physiol. **139**:693 (Sept.) 1943.

The decreased activity, poor appetite and constant state of dioestrus produced in rats by an exclusive diet of yellow corn are all corrected by giving the animals access to a solution of pure vitamin D₃. Ultraviolet irradiation of animals fed yellow corn has a similar corrective effect but to a smaller extent.

Both vitamin A acetate and a distillate of cod liver oil without any vitamin A or D were essentially without effect on the nutritive condition of rats maintained on the yellow corn diet for one hundred days. Therefore, it is concluded that the value of cod liver oil as a supplement to an exclusive diet of yellow corn is, in all probability, due to the vitamin D content of the fish oil.

Attention is called to the close similarity between the symptoms of rats on an exclusive diet of yellow corn and those of hypophysectomized rats, and the possibility was considered that vitamin D might achieve its effect indirectly through stimulation of the anterior lobe of the hypophysis.

FROM THE AUTHORS' SUMMARY.

VITAMIN A LEVELS IN MATERNAL AND FETAL BLOOD PLASMA. JANE NICHOLLS BYRN and N. J. EASTMAN, Bull. Johns Hopkins Hosp. **73**:132 (Aug.) 1943.

Samples of blood from the umbilical cords of 50 infants showed substantial amounts of vitamin A in the plasma. The average value was 91.3 U. S. P. units per hundred cubic centimeters, compared with an average maternal level, taken a few hours before delivery, of 106.3 U. S. P. units. High doses of vitamin A fed to 15 women in labor failed to raise the levels in their infants above those in untreated controls.

LYTLE, New York.

THE CONCENTRATION OF VITAMIN A IN THE BLOOD PLASMA DURING PREGNANCY. OSCAR BODANSKY, J. M. LEWIS and MICHAEL C. C. LILLIENFELD, J. Clin. Investigation **22**:643 (Sept.) 1943.

The mean concentration of vitamin A in the plasmas of 70 women who were six months pregnant or less was 105.4 U. S. P. units per hundred cubic centimeters (standard deviation of 23.2 units). The mean value for 62 women in the third trimester of pregnancy was 91.1 units per hundred cubic centimeters (standard deviation of 26.2 units) and hence significantly lower than the mean value during the first two trimesters.

The mean value of the plasma carotene during the sixth, seventh and eighth months (145.9 micrograms per hundred cubic centimeters) was significantly higher than during the first five months (111.9 micrograms per hundred cubic centimeters).

The decrease in the concentration of vitamin A in the plasma during the third trimester is probably due to storage in the fetal liver and utilization by the fetal tissues. Other possible mechanisms are discussed.

AUTHORS' SUMMARY.

THE EFFECT OF CONCENTRATION ON THE ABSORPTION OF VITAMIN A. A. GEORGE REIFMAN, LOIS F. HALLMAN and HARRY J. DEUEL JR., *J. Nutrition* **26:33** (July) 1943.

The rate of absorption of vitamin A in rats was found to be proportional to the concentration of the vitamin in the administered material. No relationship between the rates of absorption of neutral fat and vitamin A was noted. Vitamin A apparently was not destroyed by contact with intestinal bacteria for a period of three hours. FREDEEN, Kansas City, Mo.

BIOTIN CONTENT OF MEAT AND MEAT PRODUCTS. B. S. SCHWEIGERT, E. NIELSEN, J. M. MCINTIRE and C. A. ELVEHJEM, *J. Nutrition* **26:65** (July) 1943.

Of the meats and meat products tested, kidney and liver were the richest sources of biotin, as determined by the effect on the growth of *Lactobacillus casei*. Good sources were heart, pancreas and dark and light chicken meat. Beef spleen, lung, brain and tongue had about the same amount of biotin in millimicrograms per gram of fresh tissue as did lamb, beef, veal and pork muscle. Pork loins and hams averaged 50 millimicrograms of biotin per gram of fresh tissue. About 77 per cent of the biotin was retained in the meat alone after cooking and about 80 per cent in the meat plus drippings. FREDEEN, Kansas City, Mo.

THE RETENTION OF VITAMINS IN MEATS DURING STORAGE, CURING AND COOKING. B. S. SCHWEIGERT, J. M. MCINTIRE and C. A. ELVEHJEM, *J. Nutrition* **26:73** (July) 1943.

The contents of thiamine, nicotinic acid and riboflavin in fresh, fresh stored and cured hams before and after cooking were determined. The thiamine and nicotinic acid retained during storage averaged 92 per cent, and the riboflavin retained was 85 per cent. The amounts retained after curing were thiamine 73 per cent, nicotinic acid 84 per cent and riboflavin 92 per cent. After roasting, in the meat alone the average retention was thiamine 58 per cent, nicotinic acid 79 per cent and riboflavin 74 per cent; after frying, thiamine 85 per cent, nicotinic acid 85 per cent and riboflavin 77 per cent. The total retention in the meat plus drippings after roasting averaged 70 per cent for thiamine, 96 per cent for nicotinic acid and 84 per cent for riboflavin; after frying, thiamine 92 per cent, nicotinic acid 96 per cent and riboflavin 86 per cent. The over-all retention of the vitamins from fresh stored to cured fried samples agreed with the vitamin retention during curing and frying. A higher retention of thiamine in the meat alone was found after frying, as compared with roasting, braising and broiling.

FREDEEN, Kansas City, Mo.

VITAMIN K AND PROTHROMBIN LEVELS WITH SPECIAL REFERENCE TO THE INFLUENCE OF AGE. F. W. STAMLER, R. T. TIDRICK and E. D. WARNER, *J. Nutrition* **26:95** (July) 1943.

To maintain the normal level of prothrombin, young white leghorn chicks required 1 to 2 micrograms of 2-methyl-1,4-naphthoquinone per day. About one twentieth of this amount was necessary to maintain sufficient prothrombin in the blood to protect the animal from hemorrhagic manifestations. As the chick increased in age, despite the fact that the body weight increased severalfold within a few weeks, no increase in the amount of vitamin K was required. The data suggested

that a large portion of the vitamin requirement of the growing chick was associated with the increase in size.

FREDEEN, Kansas City, Mo.

THE EFFECT OF COOKING WITH AND WITHOUT SODIUM BICARBONATE ON THE THIAMINE, RIBOFLAVIN AND ASCORBIC ACID CONTENT OF PEAS. CORNELIA H. JOHNSTON, LOUISE SCHAUER, SAM RAPAPORT and HARRY J. DEUEL JR., *J. Nutrition* **26:227** (Sept.) 1943.

The addition of sodium bicarbonate to the water decreased the time necessary for the cooking of peas, both fresh and frozen. Approximately 80 per cent of the thiamine, 65 per cent of the riboflavin and 45 to 60 per cent of the ascorbic acid was retained in the peas after cooking. There were no differences from the addition of sodium bicarbonate to the cooking water. When the vitamin content of the cooked peas was added to that of the cooking water, the recovery of these three vitamins was found to be practically complete. The destruction of vitamin C by the cooking process amounted to between 15 and 20 per cent in the frozen peas, and this was not influenced by the method used. With overcooking, to the extent that the peas started to disintegrate, the losses of thiamine from both fresh and frozen peas were considerably greater and the recovery was much less. Under these conditions the destructive effect of sodium bicarbonate was somewhat greater. FREDEEN, Kansas City, Mo.

THE EFFECT OF COMMERCIAL CLARIFICATION ON THE VITAMIN CONTENT OF HONEY. M. H. HAYDAK, L. S. PALMER, M. C. TANQUARY and A. E. VIVINO, *J. Nutrition* **26:319** (Sept.) 1943.

Clarified and unclarified honey were assayed for thiamine, riboflavin, pantothenic acid, nicotinic acid and ascorbic acid. The clarified samples showed a general decrease in the concentration of vitamins, ranging from 8 to 45 per cent; however, there was no perceptible reduction in the antihemorrhagic activity of the clarified honeys compared with the unclarified controls.

FREDEEN, Kansas City, Mo.

THE B VITAMINS IN HONEY. GEORGE KITZES, H. A. SCHUETTE and C. A. ELVEHJEM, *J. Nutrition* **26:241** (Sept.) 1943.

Honey contains thiamine, riboflavin, nicotinic acid, pantothenic acid, pyridoxine, biotin, and folic acid, as determined by microchemical and microbiologic methods. A great variation in amounts was noted, perhaps due to differences in the source and number of grains of pollen present. Aged honeys revealed a decrease in the content of pantothenic acid. Pollen and royal jelly are good sources of the vitamin B complex. Royal jelly is rich in biotin and pantothenic acid, which may be significant in the metabolism of the young bee.

FREDEEN, Kansas City, Mo.

SIGNIFICANCE OF PLASMA ASCORBIC ACID LEVELS IN NEBRASKA CHILDREN. JOHN L. GEDGOUD, VIOLET M. WILDER and JOSEPH A. HENSKE, *J. Pediat.* **23:39** (July) 1943.

The level of ascorbic acid in the plasma was determined for 220 unselected Nebraska children of the lowest income group at the time of admission to the hospital. The results were classified as high (0.7 mg. per hundred cubic centimeters or more), intermediate or borderline (0.4 to 0.69 mg. per hundred cubic centimeters) and low (0.2 to 0.39 mg. per hundred cubic

centimeters). Of the children with high and intermediate levels, one third had infections. However, infection was present in two thirds of the group with low levels of ascorbic acid; the majority of these children were under 2 years of age.

"On a daily intake of 60 to 80 mg. of ascorbic acid, a level of 0.7 mg. per cent or more was attained in 81 per cent of children without infection, regardless of the entrance value.

"The ease of attaining a value of 0.7 mg. per cent or more indicated that 36.4 per cent of 'healthy' children were probably on a diet containing less than from 60 to 80 mg. daily and that levels of from 0.4 to 0.69 mg. per cent may still be considered 'borderline' for that group.

"In two healthy infants entering with plasma levels in the borderline (0.4 to 0.69 mg. per cent) zone, 60 to 80 mg. of ascorbic acid daily did not raise the level beyond 0.7 mg. per cent over observation periods of from eighteen to nineteen days. This is an incidence of two in ninety-six cases (or 2 per cent).

"Of twelve children with infections, acute and chronic, from 100 to 150 mg. ascorbic acid daily was adequate to raise the plasma level to 0.7 mg. per cent or more in eleven, over periods of from three to twenty-one days.

"Only one 'healthy' child persisted in maintaining a low level of plasma ascorbic acid or an intake of from 60 to 80 mg. daily during eleven days of observation."

SHMIGELSKY, Chicago.

INFANTILE SCURVY. DANIEL BLITZ, J. Pediat. **23:87** (July) 1943.

"The characteristic findings in the roentgenogram taken years after clinical cure are oval, definitely circumscribed areas of rarefaction found in the interior of the epiphyseal centers of ossification. These lesions are always bilateral. These centers of ossification are present in the acute stage of the illness.

"According to Steinberg and Sussman, the blood supply to these centers of ossification is not very rich and is independent of the blood supply to the diaphysis. Upon union of epiphysis with diaphysis there is a concomitant enrichment in the blood supply to the epiphyseal center of ossification and the rarefied area disappears. These investigators feel that these lesions are pathognomonic of healed pre-existent scurvy and may be confused with bone cysts. Schwartz stated that this roentgenologic sign was seen in no other condition. On the other hand, McLean and McIntosh found similar roentgenograms in two cases, one in a patient with acute lymphatic leucemia, another in a patient with anemia of the von Jaksch type. Similar roentgenograms have been found in several cases of healed rickets. These lesions in the epiphyseal centers of ossification may not be pathognomonic of healed pre-existent scurvy, but they are very characteristic of it.

"A case report is presented with the classical symptoms and typical roentgenograms of acute infantile scurvy. A follow-up roentgenogram four and one-half years after clinical cure is presented with the characteristic findings."

AUTHOR'S SUMMARY.

THE EFFECT OF SODIUM DIPHENYL HYDANTOINATE (DILANTIN SODIUM) ON THE UTILIZATION OF ASCORBIC ACID BY GUINEA PIGS. A. D. EMMETT, EVA R. HARTZLER and R. A. BROWN, J. Pharmacol. & Exper. Therap. **78:215** (July) 1943.

It is well known that the use of diphenylhydantoin sodium in treatment of epilepsy may be accompanied

by reactions in the gingiva somewhat simulating scurvy. Experimental evidence hitherto had both supported and denied the claim that the results were due to lowering of the level of vitamin C in the blood. The authors' conclusions are as follows:

"The results indicate: (a) that the dilantin sodium had little or no effect on the gain or loss in weight; (b) that the dilantin sodium treated guinea pigs were able to breed and rear their young; (c) that dilantin did not raise or lower the plasma ascorbic acid levels; (d) that the drug had no influence on the ascorbic acid content of the adrenals, brain, testes and liver; and (e) that there were no gross pathological manifestations of scurvy including gingivitis."

PILCHER, Cleveland.

THIAMIN CHLORIDE—AN AID IN THE SOLUTION OF THE MOSQUITO PROBLEM. W. RAY SHANNON, Minnesota Med. **26:799** (Sept.) 1943.

Ten cases are reported which appear to be fairly convincing in demonstrating that thiamine hydrochloride in sufficient amounts, if given by either mouth or by injection, is capable of reducing the reactions to mosquito bites. According to the author it causes a rapid recession of welts even of long standing and contributes much to the elimination of the nuisance problem which the mosquito presents. Whether or not it can contribute toward the solution of the health problem depends on many undetermined factors. STOESSER, Minneapolis.

THE ANTI-THIAMINE FACTOR IN FISH. PHILIP S. OWEN and JOSEPH W. FERREBEE, New England J. Med. **229:435** (Sept. 9) 1943.

Epidemics of a severe and an unusually fatal paralytic disturbance have been observed in animals when fish has been added to their diet.

The disease is evidently one of thiamine deficiency, since it may be produced by thiamine deficiency under experimental conditions and may be cured by injections of thiamine.

There are a number of reasons why thiamine deficiency of this particular origin may not be frequent in man. The portions of fish that are rich in the anti-thiamine factor are for the most part those usually discarded in the preparation of fish for human consumption, that is, viscera, heads, skins and scales. Moreover, the destructive reaction with thiamine is definitely extrinsic since the factor itself is destroyed by peptic digestion, by cooking or by drying.

GENGENBACH, Denver.

THE ASCORBIC ACID CONTENT OF LATE-WINTER TOMATOES. ARTHUR D. HOLMES, CARLETON P. JONES and WALTER S. RITCHIE, New England J. Med. **229:461** (Sept. 16) 1943.

The tomato is generally considered one of the most important of the protective foods, owing largely to its vitamin content. It is commonly classed as a vitamin C food and is frequently listed as one of the richest natural sources of ascorbic acid (vitamin C). Since it can be raised easily even by amateur gardeners, it is almost universally recommended for the home garden.

It is quite evident from the results of this study that the homemaker, the nutritionist and the physician must not consider late winter tomatoes as equivalent to vine-matured, sun-ripened summer tomatoes as a source of ascorbic acid for the human dietary. In computing the vitamin C value of late winter tomatoes, one should not assign to them more than one-third the value ordinarily attributed to fully ripe summer tomatoes.

GENGENBACH, Denver.

ACTION OF NICOTINIC ACID ON CARBOHYDRATE METABOLISM. F. J. NEUWAHL, *Lancet* **2**:348 (Sept. 18) 1943.

Observations were made on the action of nicotinic acid on carbohydrate metabolism in 15 nondiabetic and 12 diabetic subjects.

The depression of the blood sugar curve and the effect of nicotinic acid on the difference in the dextrose content of arterial and venous blood and on the response to injected insulin suggested that nicotinic acid may potentiate the action of insulin.

The administration of nicotinamide to diabetic persons improved the carbohydrate tolerance in every instance.

LANGMANN, New York.

Hygiene; Growth and Nutrition; Public Health

STANDARDS FOR THE BASAL METABOLISM OF CHILDREN FROM 2 TO 15 YEARS OF AGE, INCLUSIVE. ROBERT C. LEWIS, ANNA MARIE DUVAL and ALBERTA ILIFF, *J. Pediat.* **23**:1 (July) 1943.

Standards for the basal metabolism of children from 2 to 15 years of age, inclusive, have been established on the basis of 1,007 determinations on 70 normal, healthy boys and 718 determinations on 57 normal, healthy girls. In the age range from 2 to 12 years inclusive, the values reported represent the combined results of two consecutive studies of approximately five years each that were found to check each other closely. Further work is now being done to test the validity of the standards for older children.

The bases selected for the establishment of standards are calories per hour per square meter referred to age and calories per hour referred to surface area, weight and height, respectively. The first three methods were chosen because of the relatively low degree of dispersion exhibited, while the last was included because of its wide use.

The results of this study are compared with those of representative reports in the literature, and the role of relative body size in the choice of methods of reference for basal metabolism is included in the discussion.

SEMGELSKY, Chicago.

MATERNAL AND CHILD HEALTH. JAMES YOUNG, Edinburgh *M. J.* **50**:474 (Aug.) 1943.

Young emphasizes the fact that the interests of the mother and of the child are unified, forming a state of welfare which is linked by social, economic, nutritional and industrial influences with the health of the community. He discusses community health in relation to the medical schools, the university, the maternity hospital, antenatal and child welfare clinics, social service and continuity of health supervision. However, the most important subject is that of nutrition, since it is concerned with the physical and, as some believe, the mental welfare of the child. A short summary embodies the author's suggestions for bringing about the desired results.

NEFF, Kansas City, Mo.

CONTRIBUTION TO THE STUDY OF INFANTILE MORTALITY IN THE CITY OF BUENOS AIRES. F. UGARTE, *Rev. Soc. puericult.* Buenos Aires **9**:250 (July-Sept.) 1943.

The author presents a statistical picture of the mortality of children under 2 years of age, pointing to intestinal disturbances as the most important cause of death. In recent years the mortality of infants under 30 days old has been diminished considerably, but for children from this age to 2 years it has been decreased

only slightly. In the second age group a close relationship between the fluctuations in the number of deaths caused by intestinal disturbances and the seasonal variations in temperature was found; the mortality is greater as the temperature becomes higher and diminishes considerably during the winter. A suggestion is made that the death certificates of infants under 2 years of age contain an account of the feeding employed and a short history of previous illnesses.

In Argentina, as in other countries, more male than female infants are born, and among children under 2 years of age the mortality for male infants is greater than that for female infants.

BRIESES, Mexico.

TEACHING OF INFANT CARE IN GRAMMAR SCHOOL. I. PUIG, *Rev. Soc. puericult.* Buenos Aires **9**:268 (July-Sept.) 1943.

The author proposes that the care of infants should be taught at the end of the grammar school period because girls first have the maternal instinct at this age. Classes could be held in schools, and visits could be made to nurseries.

BRIESES, Mexico.

Prematurity and Congenital Deformities

INTRAUTERINE TRAUMATIC LESIONS OF THE HEART: REPORT OF A CASE, WITH AUTOPSY. W. M. SILVERNAGEL and R. S. FIDLER, *Am. Heart J.* **26**:129 (July) 1943.

The authors report a case of intrauterine cardiac injury resulting from a nonpenetrating blow to the maternal abdomen. The blow resulted in death of the fetus. The autopsy revealed hemorrhage into the epicardium along the coronary vessels and into the pericardium and pleura, together with hemopericardium and hemothorax.

GIBSON, Chicago.

STUDIES IN THE METABOLISM OF THE HUMAN PLACENTA: I. OXYGEN CONSUMPTION IN RELATION TO AGEING. H. W. WANG and L. M. HELLMAN, *Bull. Johns Hopkins Hosp.* **73**:31 (July) 1943.

The authors point out that the effect of aging of the human placenta on the child and on the mother is unknown and that no metabolic studies have been carried out on human placentas.

The oxygen consumption of the human placenta decreases gradually as pregnancy advances, and this corresponds with the histologic changes in the villi of the organ. The use of analgesics or anesthetics during labor does not influence oxygen consumption.

LYTTLE, New York.

GAIN IN WEIGHT DURING PREGNANCY. HELEN R. ROBINSON, ALAN F. GUTTMACHER, EDMUND P. H. HARRISON JR. and JOHN M. SPENCE JR., *Child Development* **14**:131 (Sept.) 1943.

In a study of 484 private patients, conducted by three physicians, the gain in weight during the period of gestation was studied and careful records were kept. The economic status of the patients was uniformly good, the women were somewhat older than the average for child-bearing women, and a rather disproportionate percentage (62 per cent) were primigravidas. As a result of the final analysis of the data (restricted to the 299 cases under longest observation) a number of significant conclusions were drawn. Among the more important observations are the following: (1) Cumulative gain in weight over the period of gestation, if

plotted, could almost be characterized as a straight line. Increase was least in the first two months and greatest in the seventh. The total average gain was 24.4 pounds. (2) There was no significant difference between the gain of the primigravida and that of the multigravida. (3) The gain in weight during pregnancy was inversely related to the usual weight of the mother. Regulation of diet according to the build of the patient was successful in controlling the gain. (4) Six weeks after delivery, the majority of the women had not yet returned to their prepregnant weight. (5) The greater the total gain during pregnancy, the greater the difference between the postpartum weight and that at the third month of gestation.

A DEFECT IN THE METABOLISM OF TYROSINE AND PHENYLALANINE IN PREMATURE INFANTS: III. DEMONSTRATION OF THE IRREVERSIBLE CONVERSION OF PHENYLALANINE TO TYROSINE IN THE HUMAN ORGANISM. S. Z. LEVINE, MARGARET DANN and ELEANOR MARPLES, J. Clin. Investigation **22**:551 (July) 1943.

Ten healthy infant boys on constant high protein, vitamin C-free diets were given various doses of levotyrosine and dextrolevophenylalanine in pure form, and the excretion of these aromatic amino acids and their derivatives in the urine was studied. In both premature and full term infants the repeated ingestion of dextrolevophenylalanine resulted in the appearance in the urine not only of this amino acid but of levotyrosine and its derivatives parahydroxyphenylpyruvic acid and parahydroxyphenyllactic acid in large amounts. The reaction is apparently irreversible as shown by the absence of significant excretion of phenylalanine and phenylpyruvic acid after ingestion of equivalent amounts of levotyrosine. Such data suggest that levotyrosine in the diet cannot replace dextrolevophenylalanine, which in animals has been shown to be essential.

Vitamin C, previously shown to diminish or abolish the excretion of aromatic metabolites after single smaller doses, was apparently ineffective when jointly given with repeated larger doses of either tyrosine or phenylalanine.

GUEST, Cincinnati.

SPINA BIFIDA AND CRANIUM BIFIDUM: I. A SURVEY OF FIVE HUNDRED AND FORTY-SIX CASES. FRANC D. INGRAHAM and HENRY SWAN, New England J. Med. **228**:559 (May 6) 1943.

During the last two decades 546 infants and children with spina bifida or cranium bifidum have been seen at the Children's Hospital in Boston.

Race, sex and economic status seem to have little bearing on the incidence of spina bifida.

In 16 (6 per cent) of the 277 cases in which information was available, the patients said there had been spina bifida in the family. Approximately an equal number reported anomalies other than spina bifida in the family.

In 232 patients, or slightly more than half the series, 570 associated anomalies were recorded. Even this large number is probably an underestimate.

A series of 462 cases of spina bifida and 84 of cranium bifidum (encephalocele) is presented, with data on the incidence, sex, race, type, site, associated anomalies and clinical manifestations.

Therapeutic indications and end results are tabulated and discussed.

The age of choice for operations on infants is between 12 and 18 months. This allows time for the develop-

ment and recognition of disabilities and hydrocephalus, for the local growth of skin adequate to permit closure and for the sufficient development of the child in stature and nutrition to present a better operative risk.

Other factors and conditions are discussed as indications for or against operation. Operative procedures are described in detail.

Thirty per cent of the patients with spina bifida and 34 per cent of those with encephalocele may expect a relatively normal life. An unduly pessimistic prognosis is therefore unwarranted until individual evaluation has been carefully made.

GENGENBACH, Denver.

SPINA BIFIDA AND CRANIUM BIFIDUM: II. SURGICAL TREATMENT. FRANC D. INGRAHAM and HANNIBAL HAMLIN, New England J. Med. **228**:631 (May 20) 1943.

This well illustrated paper shows the typical conditions before and after operative treatment of spina bifida and cranium bifidum. Preoperative, operative and postoperative techniques are illustrated and discussed in detail.

The essential features of satisfactory treatment of congenital cranial and spinal protrusions are selection of patients suitable for operation, simple removal and repair of the defect by a technic adapted to the location, size and shape of the protrusion and meticulous post-operative care. It should be emphasized that a definite hopeless prognosis should rarely be given at the first examination.

GENGENBACH, Denver.

SPINA BIFIDA AND CRANIUM BIFIDUM: III. OCCULT SPINAL DISORDERS. FRANC D. INGRAHAM and JOHN J. LOWREY, New England J. Med. **228**:745 (June 10) 1943.

According to the authors, roughly 25 per cent of normal children have occult defects in the vertebral laminae, and the incomplete closure is frequently demonstrated in roentgenograms taken for some other reason. The defect is likeliest to occur in the lumbar or sacral region and can be shown to have persisted in many normal adults.

The paper is well illustrated. The authors' summary follows:

"An analysis of 65 cases of spina bifida occulta is presented. The symptoms and usual findings are listed.

"Twenty-one cases in which laminectomy was performed are discussed, and the operative findings summarized.

"The indications for operation were specific, and operation was not performed without a definite history of progressive difficulty.

"In only 2 out of the 21 cases did operation fail to show a lesion that might account for the presenting complaint. In the large majority operation showed a definite lesion affecting the cauda equina or nerve roots, that could be remedied surgically.

"The findings suggest that probably more of the questionable cases should be offered the benefit of exploration."

GENGENBACH, Denver.

THE SIGNIFICANCE OF FETAL HICCUPS. W. A. MCGEE, South. M. J. **36**:508 (July) 1943.

The author states the belief that fetal hiccups are definitely related to allergic states in the infant and that the attending physician should keep this in mind in planning any initial feeding regimen.

SCHLUTZ, Chicago.

CONGENITAL DEFECTS IN INFANTS FOLLOWING INFECTIOUS DISEASES DURING PREGNANCY. C. SWAN, A. L. TOSTEVIN, B. MOORE, H. MAYO and G. H. BLACK, M. J. Australia 2:201 (Sept. 11) 1943.

As a result of a questionnaire sent to all medical practitioners in southern Australia the authors were enabled to study the relationship between acute exanthems during pregnancy and congenital defects in infants in 61 cases. Of the 61 infants, 36 had congenital defects. Forty-nine of the mothers had had rubella, 9 had contracted morbilli and 2 had had mumps during the period of pregnancy. Four mothers had no knowledge of any exanthem occurring during this time.

Of the 49 infants born to mothers who had rubella during pregnancy 31 exhibited congenital defects. The abnormalities included cataract (in 13 infants of whom 8 had other defects), deaf-mutism (in 7 infants, 2 of whom had associated defects), heart disease (in 17 infants, 11 of whom had associated defects), microcephaly (in 3 infants), hypospadias (in 1 infant), clubfoot (in 1 infant), mongolism (in 1 infant) and mental retardation. With 2 exceptions all of the 31 mothers with congenitally defective children had contracted rubella within the first three months of pregnancy. The mothers of 4 of the infants with congenital cataract, associated with other defects in 3 instances, denied all knowledge of an exanthem during pregnancy.

No congenitally defective babies were born to mothers who had morbilli in pregnancy. One mother who had mumps during pregnancy gave birth to a child with a congenital corneal opacity. GONCE, Madison, Wis.

MEDICOSOCIAL PROBLEM OF PREMATURE INFANTS. JUAN J. MURTAGH, Rev. Soc. puericult. Buenos Aires 9:229 (July-Sept) 1943.

The author reviews the etiologic factors in prematurity; he ascribes 10 per cent of the premature births in Buenos Aires to syphilis.

He urges that obstetricians try to diminish as much as possible the common causes of prematurity, to give to the premature infant the right care, and to cooperate with the pediatrician. The latter should care for the infant, with the aid of special nurses and of complete equipment, consisting of ambulances, incubators, oxygen tents and warm cribs. He also suggests that social workers give special advice to future mothers.

BRIEESCA, Mexico.

Newborn

PNEUMOTHORAX IN THE NEWBORN INFANT. G. W. SALMON and G. B. FORBES, J. Pediat. 23:50 (July) 1943.

Pneumothorax is not infrequent in the neonatal period and may be associated with alarming signs of respiratory difficulty. Two possible causes to be considered are (1) the presence of a pathologic condition in the respiratory tract and (2) overdistention of the alveoli. Either or both of these may weaken the walls of the respiratory tract and lead to a break in their continuity resulting in the appearance of air outside the normal pathways. Pneumothorax secondary to the first cause probably arises by a direct rupture of the visceral pleura, while pneumothorax due to the second cause is more likely to follow the mechanism described by Macklin; air travels from the pulmonary interstitial tissue to the mediastinum producing mediastinal emphysema and then ruptures the mediastinal pleura to

produce pneumothorax. In this second type the pneumothorax is more likely to be the result of the respiratory difficulty than the cause.

SHMIGELSKY, Chicago.

BRONCHOSCOPY IN THE NEWBORN INFANT. FLETCHER D. WOODWARD and WILLIAM W. WADDELL JR., J. Pediat. 23:79 (July) 1943.

When indicated bronchoscopy is a life-saving procedure. Woodward and Waddell present reports to illustrate the safety and value of bronchoscopy in the newborn infant. At present the indications for bronchoscopy in the newborn infant are not clearcut, and it is done only when the usual procedures have failed. The authors advise that bronchoscopy be used more frequently in all types of congenital atelectasis.

In 1 case described, a 5½ pound (2,495 Gm.) twin was hospitalized six hours after birth because of persistent cyanosis and dyspnea which cleared with administration of oxygen but returned when the baby was taken out of the incubator. A roentgenogram of the chest revealed collapse of the left lung with the heart and mediastinum drawn to the left. Since no improvement occurred in three days, a 3.5 mm. bronchoscope was introduced and suction was applied to the left bronchus. The procedure lasted three minutes. Prompt improvement followed and a roentgenogram taken two days later showed normal aeration.

The second case reported was that of a newborn premature infant (1,860 Gm.) with massive congenital atelectasis of the left lung due to absence of the left main bronchus. The baby was examined bronchoscopically at 9 days of age with a 3.5 mm. bronchoscope and again at 18 days of age. When the infant was 26 days old, 2 cc. of iodized poppyseed oil was injected into the trachea through a laryngoscope; roentgenograms were taken, and the oil was removed by suction. The procedure was well tolerated. The child is now 16 months old, and the left lung is still unaerated.

A case of massive congenital atelectasis of the left lung due to congenital absence of the left main bronchus in an 11 year old boy is presented because of its rarity and interest.

Cases of partial congenital atelectasis and pneumothorax in 2 newborn infants who died several hours after bronchoscopy are described. Autopsies were not permitted. In these 2 cases the procedure was well tolerated, and death was not deemed due to bronchoscopy.

SHMIGELSKY, Chicago.

TWO CASES ILLUSTRATING THE TREATMENT OF NEONATAL PNEUMONIA. R. A. RATCLIFF, Arch. Dis. Childhood 17:153 (Sept) 1942.

Two cases of neonatal pneumonia, associated with aspiration of contents of the amniotic sac and subsequent recovery, are described. The treatment is discussed with particular reference to the rapid improvement which followed injection of human serum.

KELLY, Milwaukee.

MODERN VIEWS OF JAUNDICE IN THE NEWBORN. REGINALD LIGHTWOOD, Practitioner 150:286 (May) 1943.

The author presents interesting classifications and an excellent review of fetal erythroblastosis. Of special interest are some of the references to early speculation in regard to the antigen-antibody reaction and the possibility of disease states due to it in human beings.

THELANDER, San Francisco.

Acute Infectious Diseases

STUDIES ON THE EFFECTIVENESS OF PHENOTHIAZINE IN HUMAN NEMATODE INFECTIONS. HARRY MOST, *Am. J. Trop. Med.* **23**:459 (July) 1943.

The authors experimented with phenothiazine in patients with various nematode infections. They concluded that it was effective in the treatment of human *Enterobius vermicularis* infections. A total dose of 300 mg. per kilogram of body weight administered during three days is recommended pending further investigation, as it is toxic in large doses, causing hemolytic anemia and hepatitis. It was found ineffective against infections with *Ascaris lumbricoides*, *Necator americanus*, *Strongyloides stercoralis* and *Trichocephalus trichiurus*.

BURPEE, Augusta, Ga.

CHRONIC TOXOPLASMOSIS. DAVID WEINMAN, *J. Infect. Dis.* **73**:85 (July-Aug.) 1943.

This relatively new type of infection needs no better introduction than a perusal of the author's summary, which follows:

"Immunity in murine toxoplasma infections was relative only. It resulted in recovery from the acute attack, and for a time protected against reinoculation, but did not result in elimination of the organism.

"Mice which recovered from an acute attack became chronic carriers; in some the infection was inapparent for a time, others died long after inoculation; organisms recovered from all carriers were virulent for other animals.

"The brain of the carriers was the organ most heavily and most regularly infected following any route of inoculation.

"The pathological findings in the chronic toxoplasmosis of healthy carrier mice were quite at variance with those observed in the acute disease; notably the inflammatory necrotic lesions were uncommon despite abundance of virulent organisms.

"Toxoplasmas persisted in the pseudocyst form in carrier mice. The pseudocysts provoked less tissue damage and appeared to be more resistant than single isolated parasites.

"Human chronic toxoplasmosis has not yet been demonstrated. The close correspondence between the disease in man and in animals, and the existence of healthy human parents who transmit the infection to their offspring, make it very nearly certain that chronic infections exist in man also." TOOMEY, Cleveland.

BASAL METABOLISM IN RHEUMATIC CHILDREN. EDWARD E. BROWN and VALENTINA P. WASSON, *J. Pediat.* **23**:19 (July) 1943.

Basal metabolic rates were determined by the Benedict method for 97 boys and girls with rheumatic fever, from 8 to 17 years of age. The basal metabolic rates were low in most of these children, and reached the lowest level in the spring. The rates averaged -7.6 per cent. Continuous colds during the winter and spring months are considered an important factor. The primary infection is believed to be a chronic suppurative sinusitis, and despite the removal of tonsils and adenoids the majority of the children had adenitis of the cervical, submaxillary or retropharyngeal glands in the spring when the sinusitis and rheumatic activity were at their height.

The toxins causing the adenitis "are probably responsible for damage to the thyroid gland with consequent lowering of the basal metabolic rates."

SHMIGELSKY, Chicago.

IMMUNIZATION AGAINST RHEUMATIC FEVER. VALENTINA P. WASSON and EDWARD E. BROWN, *J. Pediat.* **23**:24 (July) 1943.

To prevent recurrences of rheumatic fever, 80 children in the ambulatory stage of rheumatic cardiac disease were given intradermal inoculations of tannic acid-precipitated toxin of the N. Y. 5 strain of hemolytic streptococci. Five inoculations were given each patient during the first winter of treatment and two a year thereafter. No general reaction or abscess formation occurred. All the patients reported some itching at the site of injections and usually some local tenderness, swelling and redness.

The results of this "short method" of immunization compare well with those of the "long method," requiring at least thirty-eight subcutaneous injections of crude toxin given over a period of two years. The children benefited by this prophylactic treatment and suffered no relapses.

SHMIGELSKY Chicago.

THE SANATORIUM METHOD FOR THE CARE OF RHEUMATIC HEART DISEASE IN CHILDREN. LEO M. TARAN, *J. Pediat.* **23**:69 (July) 1943.

A sanatorium for the treatment of children suffering from acute rheumatic disease is described in detail. The institution consists of six small units each accommodating 25 children. Children 6 to 15 years of age are accepted during the active phase of the illness and treated at the sanatorium for a period of at least six months after subsidence of clinical evidence of active rheumatic disease. Definite criteria are followed in deciding the duration of the stay, but each case is judged on its own merits.

The sanatorium is fully equipped to deal with any cardiac emergency and with all types of acute rheumatic manifestations. The clinical course and results of complete laboratory tests are recorded in full detail on forms devised for a threefold purpose: (1) to obtain an accurate history of the course of the active rheumatic disease; (2) to detect early signs of reactivity, and (3) to establish criteria for rheumatic quiescence.

Therapy is based on the principle that rheumatic disease is protracted, of months' duration. A careful psychologic approach to the patient is considered of great importance. An attempt is made to adjust the professional care to the individuality of each child. An atmosphere of encouragement and hope for rapid and complete recovery is created by the carefree and undisciplined manner of the medical personnel.

Beside teaching of the children as well as occupational therapy is continued during the acute phase. The transition from activities and routines of the acute to those of the subacute and finally to those of the quiescent phase is watched carefully and conducted slowly. Finally an attempt is made to bring about an easy transition from the sanatorium to home care.

The sanatorium has a varied medical educational program. The physiologic and pathologic aspects of heart disease are studied clinically and in the laboratories. Active research is conducted along three main lines: clinical cardiology; cardiac physiology, and bacteriology and immunology.

The St. Francis Sanatorium for Cardiac Children has been established on the principle that rheumatic disease in children, in the acute stage, cannot be adequately treated under the conditions present in the usual children's hospital. The medical policies governing this institution evolved from the concepts that (a) the active phase of rheumatic disease in children is of much longer duration than the clinical signs would seem

to show; (b) the usual clinical and laboratory diagnostic criteria are inadequate in a great many cases of acute rheumatic infection; (c) the so-called subclinical phase of acute rheumatic disease deserves as much therapeutic consideration as the well known acute rheumatic arthritis or carditis, and (d) the function of the sanatorium is to attempt to prevent further cardiac damage by active treatment of acute and subacute rheumatic infection. Five years' experience at the sanatorium gives definite encouragement for continuance of the policy as formulated.

SHMIGELSKY, Chicago.

IMMUNIZATION IN PEDIATRICS. C. J. BLOOM, South. M. J. **36**:495 (July) 1943.

The author presents a good review of the origin of immunizing agents and gives an illuminating evaluation of them, showing many successes and relatively few failures. He points out that the incidences of the diseases for which the patients were immunized and the respective death rates have been notably reduced by the systematic use of these agents in children.

SCHLUTZ, Chicago.

THE ETIOLOGY OF RHEUMATISM. WALTER M. LEVINTHAL, Edinburgh M. J. **50**:415 (July) 1943.

The author is bacteriologist in the Royal College of Physician's Laboratory at Edinburgh. He reviews here the fact that the lesion of rheumatism begins locally and in the mesodermal tissues of the body; that it is always the connective tissue which is the point of attack in the involved organ, whether the manifest lesion is arthritis, fibrosis or neuritis, and that the disease is systemic in spite of the local areas involved. The morphologic pattern of the rheumatic damage to tissue began to be studied with the discovery of the Aschoff nodule. The knowledge of the pathology has grown much in the last two generations, and there is now much evidence that there is a close connection between infection and rheumatic disease. However, rheumatic symptoms may be a feature of many infectious diseases, a fact which suggests that rheumatism is an anaphylactic condition. Levinthal discusses the mechanism of anaphylaxis and concludes in his summary that both acute and chronic rheumatism are evidences of such a state, in which multiple lesions in the mesodermal system are brought about by continual antigen-antibody reactions on tissue cells.

The author is to supplement this article with a survey, in a later edition of the same journal, of the therapeutic possibilities in rheumatic disease.

NEFF, Kansas City, Mo.

Diseases of Blood, Heart and Blood Vessels and Spleen

FRACTIONATION OF THE SERUM AND PLASMA PROTEINS BY SALT PRECIPITATION IN INFANTS AND CHILDREN: I. THE CHANGES WITH MATURITY AND AGE; II. THE CHANGES IN GLOMERULONEPHRITIS; III. THE CHANGES IN NEPHROSIS. MILTON RAPOPORT, MITCHELL I. RUBIN and DORCAS CHAFFEE, J. Clin. Investigation **22**:487 (July) 1943.

In premature and full term newborn infants, older infants and young children the levels of blood fibrin were found to be constant at all ages and equal to adult values; the level of total serum protein was found to rise with increasing maturity, with both albumin and globulin fractions involved in the increase but with a proportionately greater increase in the globulin fraction.

Throughout infancy certain of the globulin fractions (probably gamma globulin) were present in lower concentrations than those found in young children.

In children with glomerulonephritis the plasma fibrin was elevated during the acute stage of the disease and returned to normal with healing; but it remained persistently elevated in the chronic phase of the disease. In acute glomerulonephritis the serum albumin was slightly lowered, but in the chronic stages both serum albumin and globulin were reduced. In acute glomerulonephritis a globulin subfraction (gamma globulin) increased, and returned to its normal level with healing, but it was reduced in value in chronic nephritis.

During the active phase of lipid nephrosis the level of the plasma fibrin was elevated while the well known reductions in total serum protein and albumin and normal or slightly elevated concentrations of serum globulin were encountered. The globulin fraction presumed to be gamma globulin was reduced during the active phase of the disease but returned to a normal value with subsidence of the acute edematous stage.

GUEST, Cincinnati.

THE ROLE OF DIETARY PROTEIN IN HEMOGLOBIN FORMATION. ALINE UNDERHILL ORTEN and JAMES M. ORTEN, J. Nutrition **26**:21 (July) 1943.

An adequate dietary intake of protein is essential for the normal formation of hemoglobin in the rat.

FREDEEN, Kansas City, Mo.

SEVERE SUBLINGUAL AND PARATRACHEAL HEMORRHAGE IN HEMOPHILIA WITH RECOVERY FOLLOWING TRACHEOTOMY. KATHERINE H. BAIRD and MEYER S. FOX, J. Pediat. **23**:90 (July) 1943.

One type of hemorrhage in hemophilia is of especial danger, that is, bleeding into the sublingual and paratracheal tissue which may produce asphyxia before the loss of blood is in itself significant.

A review of the literature reveals reports of 7 cases of such bleeding. In 4 cases the symptoms were not sufficient to warrant tracheotomy and the patients lived. In 3 cases in which tracheotomy was necessary the patients died.

The case reported is that of a 4½ year old hemophilic boy in whom a massive sublingual and paratracheal hemorrhage developed during the course of an infection of the upper portion of the respiratory system. Tracheotomy became necessary and was successfully performed, with immediate relief of the respiratory distress. Favorable progress followed the use of repeated large transfusions of blood totaling 2,850 cc.

SHMIGELSKY, Chicago.

Diseases of Nose, Throat and Ear

THE TREATMENT OF TONSILLITIS, PHARYNGITIS AND GINGIVOSTOMATITIS WITH THE BISMUTH SALT OF HEPTADIENECARBOXYLIC ACID IN COCOA BUTTER SUPPOSITORIES. SAMUEL SILBER, J. Pediat. **23**:59 (July) 1943.

Since the inauguration of the successful use of salts of bismuth in the treatment of infections of the buccal cavity by Monteiro during the past two decades, corroboration of his observations has come from many quarters. The use of various salts of bismuth, such as the subsalicylate, the subgallate and sodium iodobismuthate, in doses of 0.05 Gm. of bismuth, injected at twenty-four to forty-eight hour intervals, produced a drop in temperature within twelve to twenty-four hours, and within forty-eight to seventy-two hours recession

of symptoms and signs, including exudate, swelling, tenderness, pain and dysphagia. Marinho, Rastelli, Mangabeira-Albernaz, Stiehr, Koehler, Boese, Imhof, Vaz de Mello, Galewski and others found repeatedly that this method was effective in cases of tonsillitis, and that gingivostomatitis (Vincent's) responded more rapidly to it than to any other form of treatment. The effectiveness of bismuth compounds in the treatment of patients harboring streptococci was shown by Monteiro and by Ricquet. Lewis, however, stressed the fusospirochetal nature of tonsillar infections in reporting the rapid response of his patients, within twenty-four to forty-eight hours, to "specific treatment" with compounds of arsenic or preferably of bismuth. He expressed the hope, however, that treatment by injection might be avoided.

Silber reports the use of the bismuth salt of heptadienecarboxylic acid in cocoa butter suppositories as the ideal treatment for tonsillitis, pharyngitis and gingivostomatitis. In the size for infants the suppositories contain 0.0675 Gm. of the bismuth salt, equivalent to 0.0225 Gm. of metallic bismuth, and the dose for adults is double that for infants. He cites the use of such suppositories by Kowarz, by Algar and Weisz and by Orso with results identical with those obtained by him.

In 32 cases of infections in children, Silber reports the disappearance of symptoms within twenty-four to forty-eight hours after the beginning of treatment, deferescence beginning in twenty-four hours and being practically complete in forty-eight hours. Subjective symptoms began to disappear and there was local improvement in twenty-four hours. Exudate, swelling, pain and dysphagia disappeared as rapidly in cases in which suppositories were used as in those in which injections were given. However, by dispensing with painful injections, by avoiding the inflamed tissues of the throat, by requiring at most two treatments twenty-four hours apart, these suppositories stand out as ideal for use in children. Silber concludes that the treatment he describes for tonsillitis, pharyngitis and gingivostomatitis is to be preferred to all others, including the use of sulfonamide drugs, because (1) it is of equal or greater therapeutic value; (2) it has the advantage of ease of administration, and (3) its use reserves the sulfonamide drugs for conditions in which they are definitely indicated or specifically required and thus avoids production of sensitivity to sulfonamide compounds. The absence of local ill effects or of systemic toxic effects of bismuth increases the desirability of this choice by the additional factor of greater safety.

SEMIGELSKY, Chicago.

ACUTE LARYNGOTRACHEOBRONCHITIS IN CHILDREN. JOHN A. V. DAVIES, *New England J. Med.* **229**:197 (July 29) 1943.

In past years acute laryngotracheobronchitis has carried a mortality of 50 to 100 per cent.

It must be differentiated from simple spasmodic croup and laryngeal diphtheria, usually by its acute onset and the rapid progress of its symptoms.

Almost 50 per cent of the patients are 2 years of age and under.

There has been a tendency to consider beta hemolytic streptococci as the only organisms involved, whereas *Staphylococcus aureus*, *Haemophilus influenzae* and pneumococci are also frequently present.

Treatment may be started with sulfathiazole or sulfadiazine or with penicillin if it is available. Inhalations of cool oxygen appear more helpful than steam. All preparations should be made for tracheotomy should it become necessary, including insuring the availability of

an aspirator. The insertion of a Mosher tube into the trachea may prove a life-saving measure.

GEGENBACH, Denver.

THE USE OF SULFONAMIDES IN THE TREATMENT OF RESPIRATORY INFECTIONS IN CHILDREN. CHARLES A. JANEWAY, *New England J. Med.* **229**:201 (July 29) 1943.

What are the indications for the use of sulfonamide drugs in the treatment of infections of the respiratory tract in children? They boil down to evidence of an acute bacterial infection of the respiratory tract that is obviously spreading and is serious or potentially serious.

What drugs can be used? Sulfadiazine is obviously the most satisfactory of the sulfonamide drugs; it disturbs children as well as adults much less in every way. The sodium salt of sulfadiazine can be given parenterally with great ease, and it therefore is the ideal drug.

Sulfathiazole can be used in the same doses as sulfadiazine, except that one must remember that sulfathiazole is much more rapidly excreted and that it is therefore more difficult to maintain an adequate concentration in the child by parenteral use of the drug without getting renal complications.

The dosage in general, if one goes by rule of thumb, is approximately 1 grain (0.06 Gm.) per pound (0.5 Kg.) for the first twenty-four hours for any serious infection. If a child is seriously ill, one half to three quarters of this amount is given as an initial dose.

These drugs cannot be given satisfactorily by rectum.

GEGENBACH, Denver.

PERILARYNGEAL CYSTS. JUSTO M. ALONSO and ELIAS REGULES, *Rev. de otorrinolaring.* **3**:15 (June) 1943.

Alonso and Regules present 2 cases of perilaryngeal cysts. These are congenital laryngeal cysts or cystic laryngoceles on the inner and the upper part of the thyroid cartilage and outside of the laryngeal muscles. The principal finding is an elevation of the base of the epiglottis and the ventricular band. Both patients were treated surgically. The cysts were removed by an external incision, and there were no recurrences.

PERSKY, Philadelphia. [*ARCH. OTOLARYNG.*]

Diseases of Lungs, Pleura and Mediastinum

THE WELTMANN REACTION IN BRONCHIAL ASTHMA.

SUSAN C. DEES, *J. Allergy* **14**:469 (Sept.) 1943.

The Weltmann reaction was studied in a series of 224 persons with asthma (51 children and 173 adults).

Patients with uncomplicated asthma or asthma and another allergic disease had coagulation bands of 6, except 6 patients with intrinsic asthma due to bacterial allergy and intrapulmonary infections, who had bands of 5.

Patients with asthma and noninfectious complications had bands of 7 or greater. All patients with infections had bands less than 6, except a group of 24 patients with chronic infection. One half of these had very mild infections. The other half had, in addition to infection, some marked degree of emphysema or pulmonary fibrosis.

On the basis of the Weltmann reaction one may apparently detect the presence of infection and fibrotic change in persons with asthma. HOYER, Cincinnati.

THE USE OF AMINOPHYLLINE RECTAL SUPPOSITORIES IN THE TREATMENT OF BRONCHIAL ASTHMA.

SUSAN C. DEES, *J. Allergy* **14**:492 (Sept.) 1943.

Rectal suppositories containing 0.25 Gm. of aminophylline gave definite relief of symptoms to a group of patients with severe asthma.

The suppositories may be used at bedtime and not often than every six hours during the day.

Aminophylline may be administered by other routes or used in combination with other antispasmodics if desired. The suppositories fill the need for a drug that will act over a long period of time and that can be self administered.

HOYER, Cincinnati.

CHLORIDE METABOLISM AND PLASMA AMINO ACID LEVELS IN PRIMARY ATYPICAL PNEUMONIA. KENDALL EMERSON JR., EDWARD CHARLES CURNEN, GEORGE SWOPE MIRICK and JAMES EDWIN ZIEGLER JR., *J. Clin. Investigation* **22**:695 (Sept.) 1943.

In primary atypical pneumonia, unlike pneumococcic pneumonia, hypoaminoacidemia does not occur, and there is no significant tendency to retain salt and water in the acute stage or to excrete an excess of these substances in convalescence.

[AUTHORS' SUMMARY.]

THE OCCURRENCE OF SULFONAMIDE-RESISTANT PNEUMOCOCCI IN CLINICAL PRACTICE. MORTON HAMBURGER JR., L. H. SCHMIDT, CLARA L. SESLER, J. M. RUEGSEGER and EDNA S. GRUPEN, *J. Infect. Dis.* **73**:12 (July-Aug.) 1943.

The authors point out that pneumococci resistant to sulfonamide compounds occur rarely, if at all, in untreated patients, though pneumococci may acquire resistance during the administration of sulfonamide drugs to patients. When the course of treatment is brief, as in the routine therapy of pneumonia, resistant organisms are not frequently developed. When the treatment must be prolonged, as in the therapy of endocarditis or slowly resolving pneumonia, the development of resistant pneumococci seems to be a regular occurrence.

This may constitute a health hazard in the future, because recovery may take place despite the presence of moderately resistant organisms, and clinical cure brought about by sulfonamide compounds is frequently accompanied by a carrier state lasting weeks, months or even years.

TOOMEY, Cleveland.

SUDDEN DEATH IN INFANTS DUE TO PNEUMONIA. JOHN M. ADAMS, *J. Pediat.* **23**:189 (Aug.) 1943.

Pneumonia is probably the most important single cause of sudden death of infants thought to be essentially well. An interstitial infiltration by mononuclear cells was the most outstanding and constant histologic characteristic of the lung tissue in the cases reported. Additional prominent features were hemorrhage and edema. These changes were similar to those recorded by the author in fatal virus pneumonitis. All patients with the latter disease showed, in addition, proliferation and desquamation of bronchial and bronchiolar epithelium and the presence of cytoplasmic inclusion bodies in these cells. Rivers and Sprunt both state that a mononuclear reaction is characteristic in the acute phase of virus diseases. The absence of bacteria and the almost complete lack of polymorphonuclear leukocytes in the microscopic sections suggested a virus as the agent of infection. Additional evidence in favor of this assumption is afforded by the fact that the marked mononuclear infiltrations demonstrated were similar to those observed in experimentally produced virus pneumonitis.

SONTAG, Yellow Springs, Ohio.

MORTALITY IN ACUTE STAPHYLOCOCCAL EMPYEMA IN INFANTS AND CHILDREN. WILLIAM E. LADD and HENRY SWAN, *J. Pediat.* **23**:297 (Sept.) 1943.

Ladd and Swan reported the results of 33 cases in which patients with staphylococcal empyema were treated at Children's Hospital in Boston.

Empyema due to staphylococci is more rare than that due to pneumococci or to streptococci.

It has usually been believed that the mortality from staphylococcic empyema was far higher than that from empyema due to other organisms. Ladd and Swan pointed out that this was not true in their series except in a limited age group. There appears to be a sharp dividing line at 4 months of age, before which the mortality is extremely high and after which the mortality is low. This prominent effect of age on mortality had not previously been reported. It is also pointed out that the staphylococcic infection was more likely to be accompanied or followed by multiple complications and infections with other organisms but that this did not affect the mortality. This strongly suggested that the pathologic and immunologic response in infants under 4 months of age is quite different from that found in later age groups. In postmortem examinations it was observed that the empyema had been adequately drained and the lung had been either partially or completely reexpanded. The cause of death was in most instances a progression of the underlying staphylococcic pneumonic process associated with generalized infection.

Adequate drainage of the empyema is recommended, and it was suggested that a decrease in mortality in the future would probably result from improved therapy of the streptococcic pneumonia rather than from any change in surgical procedure.

SONTAG, Yellow Springs, Ohio.

CONGENITAL PULMONARY CYSTS. CARL C. FISCHER, FRANK TROPEA JR. and CHARLES P. BAILEY, *J. Pediat.* **23**:219 (Aug.) 1943.

The authors describe the case of an infant who showed the signs and symptoms of expansile balloon cysts of the upper and middle lobes of the right lung.

As aspiration of the air in the cysts failed to produce any improvement in the infant's condition, lobectomy was performed when the child was 4 weeks of age. The infant recovered uneventfully, with remission of all symptoms and gradual absorption of the air as indicated by the disappearance of the basal shadow revealed by roentgenograms in the area of the extirpated lobes.

A brief discussion of other possible methods of treatment is outlined, the authors concluding with a plea for the more frequent use of lobectomy as the treatment of choice for this type of congenital anomaly in infants.

SHMIGELSKY, Chicago.

CYSTIC CONDITIONS IN THE LUNG. C. ELAINE FIELD, *Proc. Roy. Soc. Med.* **36**:584 (Sept.) 1943.

Intrapulmonary cystic conditions of the lung may be differentiated into those usually considered congenital in origin and those developing after birth. The frequency of other congenital anomalies in association with cystic lungs supports the theory of congenital origin. Three cases of the congenital type in patients aged 5½, 6½ and 3½ years and 1 case of the acquired type in a girl of 11½ years are reported. The treatment of both types is discussed and roentgenograms for 2 cases accompany the report.

WILLIAMSON, New Orleans.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

SUBDIAPHRAGMATIC ABSCESS IN CHILDREN. WILLIAM E. LAED and HENRY SWAN, New England J. Med. **229**:1 (July 1) 1943.

It is generally agreed that the mortality of untreated subdiaphragmatic abscess is between 90 and 100 per cent. Fourteen patients have been seen at the Children's and Infants' Hospitals in whom an abscess in the subdiaphragmatic space has been recognized. Eleven of these were treated surgically, with 1 death; the other 3 died with fulminating infection, and at autopsy a subphrenic abscess was found in each, as one among multiple manifestations of generalized sepsis.

The present series comprises 14 patients under 11 years of age, 6 of whom were less than 2 years old. There were 9 boys and 5 girls. All but 1 of the patients were white. In 5 of the patients (36 per cent) the abscesses were secondary to suppurative appendicitis.

Exact preoperative localization of a subdiaphragmatic abscess is more difficult in children than in adults.

In surgical intervention the extrascus approach is by all odds the one of choice. Such a procedure, with the incision in the midaxillary line just below the costal margin, is advocated for use in children.

GENGENBACH, Denver.

Psychology and Psychiatry

STUDIES ON THE PROGNOSIS IN SCHIZOPHRENIC-LIKE PSYCHOSES IN CHILDREN. R. S. LOURIE, B. L. PACELLA and Z. A. PIOTROWSKI, Am. J. Psychiat. **99**:542 (Jan.) 1943.

Lourie, Pacella and Piotrowski studied 20 children who at some time before the age of 12 years experienced psychotic episodes classifiable as schizophrenia of childhood. The group comprised 15 boys and 5 girls who presented a psychotic picture characterized by deterioration from a previous level. The average period of hospitalization was ten months. The average follow-up period was eight years. At the end of the periods of observation the following levels of adjustment were observed: An apparently normal adjustment had been made by 4 patients; fair to borderline adjustments, by 5 patients, and low grade adjustments, by the remaining 11 patients. Of the last group, 3 manifested reactions of adult schizophrenia, 5 maintained their level at the time of hospitalization or deteriorated further and in 3 an organic basis was established. In the vegetative sphere, it was striking that all patients who failed to improve remained physically infantile. Anxiety when associated with resignation was of poor prognostic significance. Psychometric data with regard to intellectual and perceptual assets offered prognostic aid. The patients capable of cooperation in the Rorschach tests showed improvement. Electroencephalographic studies showed no definite correlation with the psychotic picture.

FORSTER, Philadelphia.

[ARCH. NEUROL. & PSYCHIAT.]

STREPHOSYMBOLIA: A PEDIATRIC AND PEDAGOGIC PROBLEM. CHAUNCEY W. WYCKOFF, J. Pediat. **23**:95 (July) 1943.

The term strephosymbolia, meaning mixed symbols, was first used in this capacity by Er. S. T. Crton, formerly a professor of neurology at Columbia University, in classifying certain children having difficulty

in learning to read, children who mixed up the letters or symbols in words or read the word with letters reversed or from right to left. Such children in the past have been erroneously classified as having a developmental defect called congenital word blindness. Orton contends that the basis of the difficulty is mixed cerebral dominance; these children are neither wholly right nor wholly left sided. The fact that a child may fail to learn to read although of adequate intelligence is receiving increasing attention from educators, psychiatrists and pediatricians. There are three highly developed recording mechanisms through which reading may be learned; (1) feeling or kinesthesia, which is highly developed in the blind, (2) the auditory sense and (3) the visual mechanism.

Children with mixed cerebral dominance have great difficulty in visualizing the letters and words, as the images are recorded on both sides of the brain but opposite in sign and the impression on one side must be deleted or made inactive to obtain a correct result, or else mirror reading results.

Unfortunately there is no way of ascertaining whether a child is going to have this difficulty in learning to read until he has been subjected to the test of learning for a year or two. Orton claims that 1 to 2 per cent of the school population have a very definite degree of strephosymbolia and that up to 4 per cent have mild gradations but eventually adjust themselves.

Monroe claims that 12 per cent of children of school age have some degree of this difficulty. Unrecognized and untreated, children with a severe degree of strephosymbolia may easily acquire an inferiority complex, emotional unbalance and an asocial attitude which may readily lead to delinquency. There are several tests for the detection of this difficulty. Vision, especially fusion, should be tested; auditory tests should be made if from previous examination one is not positive that the tests of laterality were conclusive.

There are numerous borderline cases in which there is no history of sidedness and results of tests appear to be negative, and yet the child has sufficient difficulty to warrant special teaching. There is only one method of teaching such children to read, that is, by the auditory or phonetic approach, supplemented by the finger or kinesthetic method. Many of the children with severe or moderately severe strephosymbolia should be taken out of school entirely for a year or more and given this special instruction by properly trained tutors.

SHMIGELSKY, Chicago.

DEMENTIA INFANTILIS WITH CORTICAL DYSRHYTHMIA. ALEXANDER KENNEDY and DENIS HILL, Arch. Dis. Childhood **17**:122 (Sept.) 1942.

A case of dementia with catatonic behavior in a 6 year old patient is described, in whom a marked cortical dysrhythmia was found on electroencephalographic examination.

The clinical similarity between this condition and the schizophrenia-like psychoses of childhood is discussed.

No definite relationship was observed between the abnormalities of the electric rhythm and the clinical state of the patient at the time of taking the records.

Abnormal electric records were obtained from both parents.

Long series of repeated electric complexes of petit mal type were recorded. Although these were of uniquely long duration, they were not accompanied by clinical attacks until the frequency of the complexes had risen to three per second.

It is suggested that some of the recorded cases of dementia infantilis may have been cases of epileptic

lementia in which the dysrhythmia was present without outward clinical manifestation. The name dementia dysrhythmica infantum might be applied to this syndrome.

KELLY, Milwaukee.

Diseases of the Ductless Glands; Endocrinology

A RAPID TEST FOR PREGNANCY GONADOTROPINS ON THE BASIS OF INDUCED OVULATION IN MICE. H. O. BURDICK, HUBER WATSON, VINCENT CIAMPA and THOMAS CIAMPA, *Endocrinology* **33:1** (July) 1943.

It is demonstrated that ovulation can be induced in mice within twenty-four hours after a single subcutaneous injection of chorionic gonadotropin.

Induced ovulation in the mouse is such a definite end point for a bio-assay that it warrants further investigation as a rapid test of the potency of gonadotropins. It appears to be of definite value as an eighteen to twenty-four hour test for pregnancy.

JACOBSEN, Buffalo.

INHIBITION OF ESTROGENIC EFFECTS ON THE REPRODUCTIVE SYSTEM OF THE MALE RAT BY TESTOSTERONE INJECTIONS. CHARLES K. WEICHERT and HENRY B. HALE, *Endocrinology* **33:16** (July) 1943.

It is demonstrated that in rats testosterone prevents diethylstilbestrol from exerting its effects. The experiments suggest that as the normal animal gets older it loses its capacity to respond to estrogenic stimulation because of the gradual increase in secretion of androgen by the intact testes.

JACOBSEN, Buffalo.

BENEFICIAL EFFECT OF ESTROGENS ON ALTITUDE TOLERANCE OF RATS. BERNARD D. DAVIS and BENJAMIN F. JONES, *Endocrinology* **33:23** (July) 1943.

Injection of diethylstilbestrol and estradiol benzoate increased the survival rate of normal adult male rats exposed to simulated high altitudes under critical pressure-time conditions. Because a similar beneficial effect was noted in adrenalectomized rats as compared with controls, it is concluded that the beneficial effect of diethylstilbestrol is not mediated exclusively by the adrenal glands.

JACOBSEN, Buffalo.

ANDROGENS AND EXPERIMENTAL MENSTRUATION IN THE MONKEY. FREDERICK L. HISAW, *Endocrinology* **33:39** (July) 1943.

Evidence is furnished that testosterone propionate has a weak progesterone-like action on the reproductive tract of the castrated and of the intact immature female monkey.

JACOBSEN, Buffalo.

THE EFFECT OF TESTOSTERONE AND ALLIED COMPOUNDS ON THE MINERAL, NITROGEN AND CARBOHYDRATE METABOLISM OF A GIRL WITH ADDISON'S DISEASE. NATHAN B. TALBOT, ALLAN M. BUTLER and E. A. MACLACHLAN, *J. Clin. Investigation* **22:583** (July) 1943.

Clinical and metabolic studies of the effect of various hormones on an 8 year old girl with moniliasis, Addison's disease and idiopathic hypoparathyroidism are reported. These studies reveal that the administration of either methyl testosterone or testosterone propionate in addition to maintenance doses of desoxycorticosterone acetate and sodium chloride resulted in: (1) a gain in body weight; (2) a diminution in the urinary excretion

of nitrogen, potassium and sodium, and (3) a definite fall in the serum potassium concentration. No significant changes in fasting blood sugar concentration were noted. The administration of anhydrohydroxyprogesterone or of methyl androstendiol under similar circumstances prompted a decrease in urinary excretion of nitrogen but did not induce a prompt gain in body weight.

Methyl testosterone therapy did not prevent the development of symptoms and signs of acute adrenal cortical insufficiency when desoxycorticosterone acetate was withdrawn. On the other hand, testosterone propionate relieved the patient of all signs and symptoms of acute adrenal insufficiency after the discontinuation of desoxycorticosterone acetate therapy.

The lowering in the concentration of serum potassium while the patient was receiving testosterone was not associated with clinical evidences of muscular weakness or paralysis. On the contrary, the patient seemed to benefit from the testosterone as evidenced by gain in weight, growth in stature and apparent increase in strength and endurance.

[FROM THE AUTHORS' SUMMARY.]

Diseases of the Eye

NEVUS FLAMMEUS ASSOCIATED WITH GLAUCOMA; REPORT OF A CASE IN WHICH CYCLODIATHERMY WAS USED IN AN ATTEMPT TO CONTROL THE INTRAOCULAR PRESSURE. B. Y. ALVIS and V. A. TOLAND, *Am. J. Ophth.* **26:720** (July) 1943.

A boy aged 14 years had a nevus flammeus on the right side of the face which conformed in outline with the cutaneous distribution of the ophthalmic and maxillary branches of the right trigeminal nerve. The nevus was also present on the mucous membranes of the nose and throat and followed the same distribution. The right eye showed hydrophthalmos, with a tension of 43 mm. of mercury (Schiotz). There was deep, glaucomatous cupping of the optic nerve. A corneoscleral trephine was done, but the opening closed. Vogt's cyclodiathermy was then carried out. About six months later the tension was 16.5 mm. of mercury, and corrected vision was 5/75. A Bjerrum scotoma was present in the field of vision.

W. ZENTMAYER. [ARCH. OPHTH.]

PIGMENTATION OF OPTIC DISK. DANIEL KRAVITZ, *Arch. Ophth.* **29:826** (May) 1943.

Congenital pigmentation of the optic disk is uncommon in the white race, but, according to Oguchi, it is rather frequent in the Japanese. Kravitz describes the fundi in 3 cases and agrees with the opinions expressed by Duke-Elder and Mann that the pigment is the result of primitive cells of the optic stalk having regressed and acquired characteristics of pigment-forming cells in a place where other functions should have developed.

SPAETH, Philadelphia.
[ARCH. NEUROL. & PSYCHIAT.]

PEDAGOGIC VALUE OF ACTIVITY AND ITS CONSIDERATION IN THE EDUCATION OF THE BLIND. GREGORIO B. PALACIN IGLESIAS, *Bol. Inst. internac. am. de protecc. a la infancia* **15:569** (April) 1942.

If intelligence is, as it has been stated, in a certain way the result of experience, that is, the result of the continuous assimilation of things by the mind and the adaptation of this assimilation to life, persons blind from birth or from the first years of life must be placed

in contact with the things of nature as soon as possible, so that by means of the stereognostic sense those impressions that will yield a mental synthesis most fruitful to reality and that will act as a substructure for all future mental activity can be transmitted to the brain.

According to this idea parents should avoid the habit of encouraging the quietness of the blind child and arguing that he might stumble and fall or that he needs a person to care for him. On the contrary they should incite him to act, run and play as soon as he starts walking; if possible a place in the yard, garden or field (if he lives in a rural area) should be destined for the child, in which with hygienic conditions he may play and even throw himself on the ground.

To make an adequate selection of games it is sufficient to bear in mind that, as in the case of children with sight, from 5 to 7 years is the age of the evolution of self concentration and that from 7 to 10 years of age the spirit of sociability develops.

The exercise of touch and the training of the hand should begin at the age of 3, with utilization of the material that Dr. Montessori employs in "The Children's Houses." Handicrafts have a considerable creative value, but these should not be systematized before the age of 6 or 7 years.

The introduction of agriculture and gardening and those corresponding workshop activities suitable to the blind, as for instance carpentry, have a considerable creative value but should be put off until the age of 9 or 10 years in order not to give the child a professional character until the age of 12.

FROM EDITOR'S SUMMARY.

Skin Diseases; Allergy

A CASE OF JUVENILE XANTHOMATOSIS. FREDA K. HERBERT, Arch. Dis. Childhood 18:41 (March) 1943.

A case of juvenile xanthomatosis is reported, with arrested growth, enlargement of the liver and the spleen, renal disease with hypertension and enormous increases in plasma phospholipins and cholesterol.

The abnormalities in plasma and tissue lipids in various pathologic syndromes and the classification of xanthomatous diseases are discussed, and the case is compared with others reported in the literature.

KELLY, Milwaukee.

A CLINICAL NOTE ON TWO CASES OF ACANTHOSIS NIGRICANS. G. A. GRANT PETERLIN and E. COLIN JONES, Brit. J. Dermat. 55:185 (July) 1943.

The authors report 2 cases of acanthosis nigricans of the benign or juvenile form. There was no evidence of a malignant growth or of tuberculosis in either case. The cases are reported because of the rarity of this disease and because both patients were observed in a military hospital for patients with dermatologic diseases.

BLUEFARB, Chicago. [ARCH. DERMAT. & SYPH.]

THE CURE OF SCABIES AND A NEW REMEDY. G. H. PERCIVAL, Brit. M. J. 2:451 (Oct. 17) 1942.

The cure of scabies depends on the absence of lesions and itching and the failure to find the parasite for a period of about two weeks. It is advised that a 5 per cent solution of tetraethylthiuram monosulfide is capable of curing human scabies. It is nonirritating to the human skin, and no instance of idiosyncrasy has been encountered. It is cheap and clean and does not have an objectionable odor. Its trial on a more extensive scale is suggested.

BIRDSONG, Charlottesville, Va.

Teeth and Dentistry

A PHYSICIAN LOOKS AT SCHOOL DENTAL PROGRAMS. GEORGE M. WHEATLEY, Am. J. Pub. Health 33:120 (Feb.) 1943.

The author reviews experiences with the development of an economical school dental program among 6,410 children in eight schools for the 1937-1938 school year (Astoria School Health Study). The school principals sent a letter to the parents of each child advising that the child have a dental examination. The private dentists serving this area agreed to give a dental examination to any child coming to their offices accompanied by a parent. Five thousand, six hundred and eighty-one pupils (88 per cent of the total) were examined. Twenty-one per cent of the number examined needed no treatment. Parents of 1,859 children (29 per cent of the total) took no action. Twelve per cent did not consult a dentist, and 17 per cent did not obtain the recommended treatment. Private dentists examined two thirds of the school children registered, supplied almost three quarters of the treatment services and were responsible for 82 per cent of the patients' completing treatment. The younger the child, the less successful was this plan. Only 56 per cent of the kindergarten group reached a dentist, whereas at least 90 per cent of the pupils above the fourth grade received dental examinations. Another study is quoted which indicates that this record can be improved by means of a personal interview with those parents who do not respond to a written note. This supplementary interview, with a dental hygienist or some school health worker, is probably necessary in the younger age groups.

The author believes that dental examinations of school children should be done in the dentist's office rather than in the school, since 80 per cent to 90 per cent will require treatment, which is usually given in the dentist's office. This plan does not increase the school health budget, utilizes the dentists of the community in the school program, trains the pupils to seek treatment facilities in the community and impresses them with the idea that payment for dental care is worth while.

PLATT, Gouverneur, N. Y.

VARIATIONS IN CALCIFICATION AND ERUPTION OF THE DECIDUOUS AND THE PERMANENT TEETH. JOHN C. BRAUER and MASSIS A. BAHADOR, J. Am. Dent. A. 29:1373 (Aug.) 1942.

This is a consideration of calcification and eruption age in relation to chronologic age and clinical problems. Roentgenograms of the dentitions of 415 children drawn from four groups (diabetic, general hospital group, congenitally syphilitic and presumably well) were appraised against the chart of Schour and Massler. No difference among the four groups with respect to calcification and eruption was apparent. Sixty-six per cent of the children had average schedules of calcification and eruption, when considered separately.

WYLIE, San Francisco. [ANGLE ORTHODONTIST]

FURTHER STUDIES ON THE ROLE OF VITAMIN D IN THE NUTRITIONAL CONTROL OF DENTAL CARIES IN CHILDREN. E. C. McBEATH and W. A. VERLIN, J. Am. Dent. A. 29:1393 (Aug.) 1942.

Observations on five groups of children of 40 each indicate that vitamin D in the form of cod liver oil is effective in reducing the incidence of dental caries; irradiated ergosterol per U. S. P. unit does not have

an effect equal to that of cod liver oil. The authors point out that in previous favorable reports on vitamin D in relation to caries cod liver oil has been used, while unfavorable ones have been based on investigations with ergosterol.

WYLIE, San Francisco. [ANGLE ORTHODONTIST]

A CLINICAL AND ROENTGENOGRAPHIC STUDY OF PERIODONTIC PROBLEMS IN CHILDREN WITH SYSTEMIC DISEASE. C. HARLAN BLACKSTONE, J. Am. Dent. A. 29:1664 (Sept.) 1942.

This is a discussion of the soft tissue and the alveolar bone conditions in patients with mild diabetes mellitus, congenital syphilis, scurvy and aplastic anemia, supplemented with roentgenograms, case reports, photographs and a bibliography.

WYLIE, San Francisco. [ANGLE ORTHODONTIST]

CORRELATION AND COMPARISON OF LABORATORY FINDINGS WITH THE CLINICAL EVIDENCE OF CARIES ACTIVITY IN A GROUP OF SIXTY-SIX CHILDREN. MARSHALL L. SNYDER, J. Am. Dent. A. 29:2001 (Nov.) 1942.

The group was studied a little longer than two years in an effort to correlate lactobacillus counts and production of acid (reflected by changes in color in bromocresol green dextrose agar) with caries activity found in clinical examinations. The results suggest that a dentist might well rely on routine culturing of saliva specimens for determining caries activity rather than on single clinical examinations. When caries activity is marked, changes in color appear in twenty-four hours; when it is questionable, changes are seen in forty-eight hours; when it is absent, no color changes appear in seventy-two hours. There is a general relationship between rate of change in color and number of lactobacilli per millimeter of saliva, but numbers alone are not the controlling factor. The colorimetric technic possesses the advantages of simplicity, rapidity and accuracy.

WYLIE, San Francisco. [ANGLE ORTHODONTIST]

DENTAL CONDITIONS IN WHITE AND INDIAN CHILDREN IN NORTHERN WISCONSIN. LESLIE W. FOSTER, J. Am. Dent. A. 29:2251 (Dec.) 1942.

White and Indian children having comparable geographic environment are compared; differences with respect to incidence of dental caries and of malocclusion are so slight as to lead the author to conclude that while the Indians have a slight edge their contact with civilization is rapidly eliminating whatever differences may have once existed.

WYLIE, San Francisco. [ANGLE ORTHODONTIST]

Miscellaneous

SULFAMERIZINE (2-SULFANILAMIDO-4-METHYLPYRIMIDINE): I. A COMPARISON OF SULFAMERIZINE WITH SULFADIAZINE ON THE BASIS OF ABSORPTION, EXCRETION AND TOXICITY. A. D. WELCH and others, J. Pharmacol. & Exper. Therap. 77:357 (April) 1943.

In an extensive study on experimental animals and on human beings it was found that sulfamerazine is more rapidly absorbed and more slowly excreted in a more soluble form by the kidneys than sulfadiazine. In a group of men an average level of 8 mg. per hundred

cubic centimeters of blood was obtained in two hours and 10 mg. per hundred cubic centimeters was obtained in four hours from the small dose of 0.05 Gm. per kilogram (3.5 Gm. or 53 grains for a 150 pound [68 Kg.] man). A level of 6 mg. was maintained for twenty-four hours thereafter. These levels are much higher than those with sulfadiazine.

The possibility is offered that one or two doses of sulfamerazine daily may be sufficient to maintain a safe and an adequate concentration of the drug in the blood and the other tissues. The rapidity of absorption suggests that intravenous injection may not be necessary when it is desired to produce an adequate concentration in the blood quickly.

PILCHER, Cleveland.

METHYL SALICYLATE POISONING. ROBERT A. MACCREADY, New England J. Med. 228:155 (Feb. 4) 1943.

The danger of poisoning by oil of wintergreen (methyl salicylate) has not been sufficiently emphasized. It is commonly used in the home and may be accidentally ingested by children, who may associate the pleasant aroma with wintergreen-flavored candy.

The usual more severe course involves vomiting, hyperpnea, diaphoresis, extreme thirst, dehydration, stupor and convulsions. In the fatal cases death commonly occurs within twenty-four hours.

Ordinary vomiting does not completely remove methyl salicylate from the stomach. Gastric lavage should be done when the patient is first seen and should be prolonged until no trace of the odor of the drug is present in the washings. If the tube is not tolerated, an automatic lavage should be employed; that is, the patient should be forced to drink huge quantities of water or of a dilute solution of sodium bicarbonate, with consequent induction of vomiting. To be adequate the process must be repeated again and again.

Of the 5 patients reported on, a boy aged 2 years was discharged on the third day; a man aged 55 recovered; a girl aged 2 years was discharged on the third day; a boy aged 3 years died two hours after ingestion; a woman aged 48 was discharged on the seventh day.

GENGENBACH, Denver.

THE NUTRIENT ENEMA. J. W. A. MACKENZIE, Arch. Dis. Childhood 18:22 (March) 1943.

Dextrose, sodium chloride and predigested protein are absorbed from solutions introduced into the lower part of the bowel.

There is great variation in the amount of dextrose absorbed.

Absorption of sodium chloride when given by rectum is almost as great as when given by mouth.

Considerable quantities of predigested protein are absorbed from the enema.

KELLY, Milwaukee.

ABSORPTION OF DRUGS FROM THE RECTUM. J. W. A. MACKENZIE, Arch. Dis. Childhood 18:28 (March) 1943.

The absorption of potassium bromide, sodium salicylate and sulfanilamide given per rectum has been studied.

It has been shown that when given in solution all these substances are readily absorbed from the rectum. Absorption of sulfanilamide from suppositories is poor.

Absorption of sulfanilamide is slower when the drug is given per rectum than when it is given orally.

KELLY, Milwaukee.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

HEYWORTH N. SANFORD, M.D., *President, in the Chair*

Feb. 15, 1944

A Further Report on Diphtheria-Toxoid-Pertussis Vaccine, Mixed, as an Immunizing Agent. DR. LOUIS W. SAUER and (by invitation) DR. WINSTON H. TUCKER.

In 1941 we reported before this society on the use of diphtheria toxoid and pertussis vaccine, injected either separately (simultaneously) or mixed. In the early study the 464 infants who were given the injections were all over 7 months of age. Follow-up Schick tests gave negative results for 98 per cent of the infants who had been given the toxoid and the vaccine separately and for 95 per cent of those who were given the mixed antigens. Complement fixation for pertussis was 3 plus or 4 plus in 91 per cent of the former group and in 73 per cent of the latter. Children whose initial reaction was less than 3 plus had a 3 plus or 4 plus reaction three weeks after receiving a "stimulating" dose of pertussis vaccine (2 cc. of vaccine containing 15,000,000,000 bacilli per cubic centimeter). No child who received the vaccine and toxoid is known to have acquired either disease.

The present study is a continuation of the former, and includes observations on the effects of an alum-precipitated mixture. The intervals between the doses, the total amount given and the interval between the final dose and the test of immunity were varied. Injections were started after the seventh month of life; the average age was about 8 months. More than 900 additional infants were given injections at St. Vincent's Infant and Maternity Hospital and at the Evanston Health Department Clinic. Schick tests and complement fixation tests for pertussis were performed for 729 of the infants at various intervals after the last inoculation.

For the first group diphtheria toxoid and pertussis vaccine (15,000,000,000 bacilli per cubic centimeter) were injected separately (simultaneously). The three doses were injected at intervals of one week at St. Vincent's Hospital and at intervals of three weeks at the Evanston Health Department Clinic. The reaction to the follow-up Schick test was negative in 91 per cent of the children who received inoculation at one week intervals and in 97 per cent of those who received them at three week intervals. Complement fixation for pertussis was positive (3 plus or 4 plus) in 69 per cent of the children inoculated at intervals of one week. Seventy-one per cent of the children showing initial reactions that were less than 3 plus had 3 plus or 4 plus reactions after receiving a "stimulating" dose of 2 cc. of pertussis vaccine (15,000,000,000 bacilli per cubic centimeter). Pertussis complement fixation was positive (3 plus or 4 plus) in 97 per cent of the infants inoculated at three week intervals. Children who showed initial reactions that were less than 3 plus had 3 plus or 4 plus reactions after receiving a "stimulating" dose of pertussis vaccine (2 cc. of vaccine containing 15,000,000,000 bacilli per cubic centimeter).

For the second group the diphtheria toxoid and pertussis vaccine (15,000,000,000 bacilli per cubic centimeter) were mixed. The injections were given at intervals of one week at St. Vincent's Hospital and at intervals of three weeks at the Evanston Health Department Clinic. The reaction to the follow-up Schick test was negative in 91 per cent of the children inoculated at intervals of one week and in 97 per cent of those inoculated at intervals of three weeks. Complement fixation for pertussis was 3 plus or 4 plus in 66 per cent of the infants who received injections at one week intervals. Because the response to immunization in this group was low, inoculation at intervals of one week was discontinued. A total of 6 cc. of toxoid and vaccine (1, 2, 3 cc. or 2, 2, 2 cc.) when injected at intervals of four weeks gave approximately the same immunity as 7 cc. injected in three doses at intervals of three weeks. Pertussis complement fixation was 3 plus or 4 plus in 72 per cent of the infants given injections at three week intervals. Ninety-five per cent of those whose reaction was less than 3 plus had 3 plus or 4 plus reactions after receiving a "stimulating" dose of pertussis vaccine (2 cc. of vaccine containing 15,000,000,000 bacilli per cubic centimeter). In no instance was a local or systemic reaction severe.

For the third group an alum-precipitated mixture of diphtheria toxoid and pertussis vaccine (10,000,000,000 bacilli per cubic centimeter) was used. One cubic centimeter was injected three times in alternate arms at intervals of one week at St. Vincent's Hospital and at intervals of three or four weeks at the Evanston Health Department Clinic. The reaction to the Schick test was negative in 83 per cent of the infants inoculated at intervals of one week and in 98 per cent of those inoculated at intervals of three weeks. Complement fixation for pertussis was positive (3 plus or 4 plus) in 77 per cent of the one week interval group and in 92 per cent (or 94 per cent) of the three week interval group. Eleven infants at St. Vincent's Hospital had a total of 14 sterile abscesses, and 8 at the Evanston Health Department Clinic had sterile abscesses in spite of deeper injections. All infants with reactions of less than 3 plus to the complement fixation tests had 3 plus or 4 plus reactions after receiving a "stimulating" dose of 2 cc. of pertussis vaccine (15,000,000,000 bacilli per cubic centimeter).

Conclusion.—The length of the interval between the doses had a definite effect on the degree of immunity developed. In each of the three groups (those receiving separate toxoid and vaccine administered simultaneously, mixed antigens and alum-precipitated mixed antigens) the Schick test and the complement fixation test for pertussis showed that the immunity was higher when the doses were injected at three or four week intervals than when they were injected at one week intervals. The immunity as revealed by Schick tests and by complement fixation tests for pertussis was not as high after the administration of mixed diphtheria toxoid and pertussis vaccine as when the antigens had been injected separately or when the alum-precipitated

mixture had been used, but no child given plain or alum-precipitated mixed antigens since 1938 is known to have contracted either disease. The fact that 6 per cent of the 339 infants given injections of alum-precipitated mixture had sterile abscesses makes us favor plain mixed antigens. A "stimulating" dose of 2 cc. of plain pertussis vaccine (15,000,000,000 bacilli per cubic centimeter) produced a sharp increase in pertussis complement fixation. The "stimulating" dose may be injected months after the original immunization. An opportune time may be when the child is vaccinated against smallpox or when he enters nursery school or after known exposure.

Retrolental Fibroplasia. T. L. TERRY, M.D. (by invitation).

The presence of embryonic connective tissue in the meshwork of the persistent hyaloid arterial system behind the crystalline lens as a result of improper development of the inner eye is a disease entity which I call "retrolental fibroplasia." The condition usually develops three to five months after birth in extremely premature infants. It occurs in some 12 per cent of infants whose weight at birth is 3 pounds (1,300 Gm.) or less, according to Dr. Stewart Clifford. Ninety-seven cases have been recorded. The basis for the disease in the premature infant lies in the fact that the hyaloid vascular system is still functioning at birth if the infant is even four weeks premature.

The cause for the vascular persistence and the development of embryonic connective tissue has not been found, although diligent search has been made, with consideration of all logical factors, including precocious exposure to light, low postnatal temperature, Rh factor, vitamins, hemorrhage and many others.

Repeated attempts to produce this disease or to cause precocious disappearance of the hyaloid vascular system in literally hundreds of young opossums (while within the marsupial pouch) and newborn rats have failed.

Because of sluggish resorption of this abnormal tissue, retardation of growth of the eye and complications such as glaucoma and separation of the retina, the ultimate prognosis for vision is extremely bad. Radical surgical procedures and roentgen therapy have proved harmful. However, surgical attempts to produce a better blood vascular connection to the ciliary body appear to give some beneficial effect.

The discovery of a method of prevention and a possible cure probably depends on establishment of the cause, for which the pediatrician may be in a better position than the ophthalmologist.

DISCUSSION

DR. E. V. L. BROWN: Fibroplasia is difficult to differentiate from glioma (neuroblastoma) retinae. The chief symptom of both conditions is a white reflection behind the pupil. This condition is usually first observed by the mother four to six months after birth and comes from vascular tissue behind the lens.

From 1935 through 1940, 21 eyes were removed for glioma at the University of Chicago Clinics on my advice. Four of these were fibroplastic, and possibly 2 others were.

In the past three years Dr. Terry has seen 99 fibroplasias in prematurely born infants in and around Boston. According to him, 1 out of 10 babies born before the seventh month and weighing less than 3½ pounds (1,500 Gm.) is blind from fibroplasia in one or both eyes. Incubator care, widely introduced in

the early 1930's, has doubtless saved many babies; but nature seems to exact a high price in this matter, a price mitigated only a little by the fact that now, through Dr. Terry's discovery of the relationship of prematurity to fibroplasia, we are able to avoid the needless enucleation of some already blinded eyes.

DR. J. M. DONEGAN: It should be emphasized, I believe, that this condition is not simply a rare and interesting anomaly which occurs in Boston. Several months ago I had the pleasure of visiting Dr. Terry and seeing the intensive clinical and laboratory investigation he has been conducting. After he had shown me 16 infants with various manifestations of this disease, I was certainly convinced that it occurred there. Many ophthalmologists in Chicago, including Drs. Gamble, Gifford, Gradle, Kronfeld, Krause, Fowler and Allen, can attest that it occurs here with considerable frequency.

Since Dr. Terry's original paper appeared, the majority of ophthalmologists have seen examples of this condition. Prior to that time undoubtedly the condition was not recognized in many instances. Several of the eyes I have examined contained fibroblastic overgrowths behind the lens rather than retinoblastomas. These eyes had been clinically diagnosed as involved by neuroblastoma retinae and were enucleated from premature infants born as long ago as 1935. It is hoped that once this condition has been brought to the attention of the pediatricians and they have become interested in the problem much more can be accomplished in determining the cause, the frequency and the real nature of the disease.

Through Dr. Sanford's interest and help, we at Presbyterian Hospital have been studying all prematurely born infants weighing less than 5 pounds (2,250 Gm.) at birth. An attempt is made to follow these infants from shortly after birth, with particular reference to the amount of vision determinable, the relative size of the globe and the cornea, the depth of the anterior chamber, the color and development of the iris, the presence of vascular remnants on the iris, the size and reaction of the pupil, the clarity of the media, the persistence of any or all portions of the hyaloid system and the appearance of the fundus. In time we hope to obtain some clue to the causation and manner of development of the disease. Prophylactic and therapeutic measures must, of course, await future developments.

DR. EARLE B. FOWLER: I have been interested in these cases because shortly after reading the first published report I observed a patient with this condition at Presbyterian Hospital, and fairly recently I saw a second patient. Of course I am now interested in every premature infant arriving there. I wonder how many more premature infants are saved now as compared with former years. Can it be presumed that this condition is seen more often because earlier premature infants are now saved, or is it a new disease?

DR. JULIUS H. HESS: I must confess that I have seen a good many premature infants weighing less than 3 pounds (1,300 Gm.) at birth, and it is surprising how few bad eyes there were among them. In 1 infant weighing 2 pounds 10 ounces (1,200 Gm.) at birth, I noted a condition involving both eyes which might have been that described by Dr. Terry. It was first noted when the infant was 5 months of age. Dr. Terry had an opportunity to see this child today and might give an opinion. But it is remarkable how few patients I have seen personally that might fit into the

group, notwithstanding the fact that I have followed for a number of years a large group of premature children, some of whom are now 16 or 17 years old.

Is it possible that the endocrine system may be an important factor in development of the condition?

DR. SANFORD GIFFORD: I think I have seen retrolental fibroplasia in as many as 25 infants. The condition occurred unilaterally in 1 infant born at full term; there was an opaque mass behind the crystalline lens, which at the time was considered to be a glioma, and the eye was enucleated. That case was reported. When the true nature of the condition was understood, after enucleation, a review of the record showed that the cornea in this eye had been observed to be smaller than that in the other eye. It seems to me that one can be sure that an abnormally small eye does not contain a glioma.

Since Dr. Terry has been writing about fibroplasia in premature infants, I have seen about 20 patients with the disease in the Chicago area. There were 3 or 4 each at the County Hospital and at the clinics of Northwestern University Medical School, and I have seen a number in consultation. Some of the patients were brought because of the diagnosis of glioma, for which enucleation had been recommended. I have seen enough clearing in 1 or 2 patients to permit the observation of the retinal folds that Dr. Terry has described, but in most instances the membrane has been so dense that it was difficult to see the retina.

DR. HEYWORTH N. SANFORD: Referring to Dr. Fowler's question as to whether this is a new disease or whether more premature infants are being saved: When Ethel Dunham made her survey of premature infants, published in 1935, she found that the average mortality for premature infants in hospitals throughout the United States in the early 1930's was about 26 per cent. In Chicago from 1931 to 1937 the mortality for premature infants at Lying-In Hospital was 20.7 per cent. Since 1938 there has been a drive in Chicago to lower the mortality in this group of infants. I do not know the percentage for the past year, but I venture to say that certainly in most hospitals in Chicago it is well below 20 per cent; most of the decrease has been in the group of extremely small premature infants, those weighing less than 3 pounds (1,300 Gm.). Premature infants that once would have been born in hospitals without facilities for special care or in homes and would have died shortly are now taken to hospitals with special units for the care of premature infants and are saved. I wonder if there are not more early premature infants to study under today's conditions.

DR. THEODORE L. TERRY: Dr. Fowler suggests that perhaps this fibroplasia is not a new disease. That

may well be true but if so the disease entity was formerly incompletely described, and many of the symptoms of the condition have only recently been observed. The decrease in the mortality of prematurely born infants may explain the apparent "epidemic" of the condition. Although I know little of the technicalities of keeping premature infants alive, I had gained the impression, which appears erroneous, that there had been no important advances in saving premature infants during the past ten years, although I was aware that the technic was improving. Certainly this disease is much more frequent in the past five years than in the preceding four. I am sure that an ophthalmologist who saw more than 1 premature infant with this disease within twelve months could not help but realize that the condition was related to prematurity.

That Dr. Hess has seen few cases brings to mind the possibility that this condition may originate only in certain hospitals. For instance Goldberg in Baltimore found 6 cases in 1 hospital, and so far as he knew no other cases had arisen in that city at that time. Can this mean that there are certain local hospital practices which may induce the disease? The patient Dr. Hess was kind enough to let me see this afternoon had an immature cataract of rather rare type as the cause of poor vision. The condition is probably related to a disturbance of calcium metabolism and possibly had its beginning during or before the third month of fetal development. At a somewhat more advanced stage this cataract would give a picture similar to that of fibroplasia.

Consideration has been given to endocrine disturbances as a cause for retrolental fibroplasia. The premature infant living outside of a maternal environment may have endocrine dysfunction of important amount. Only recently I have learned from Dr. Snyder of the department of anatomy of Harvard Medical School—whom some of you perhaps knew when he was at the University of Chicago—that he is convinced that endocrine function begins when the endocrine glands have reached histologic maturity. Since I have obtained this information only recently, I have had no opportunity to reevaluate the endocrine factor in relation to this disease.

I am surprised at the number of cases Dr. Gifford has observed. He brings out, as did Dr. Brown, the tremendous importance of arriving at the proper diagnosis in order to avoid needless enucleation and perhaps to retain for the infant some vision.

Thank you for the opportunity of letting me describe my impression of this disease. Of course time will show which of my assumptions are incorrect.

Book Reviews

The Kenny Concept of Infantile Paralysis and Its Treatment. By John F. Pohl, M.D., and Sister Elizabeth Kenny. Price, \$5.00. Pp. 366, with illustrations. St. Paul: Bruce Publishing Company, 1943.

It is difficult to evaluate the methods recommended for the treatment of infantile paralysis in this book by Sister Kenny and Dr. Pohl. Only time can do this. However, some facts are obvious. Sister Kenny has demonstrated that immobilization in the acute stage of the disease is unnecessary. This idea is not original; others have urged that immobilization be discarded. Some men in the United States have been treating their patients without immobilization for years, although this practice had never been accepted by the medical profession until the advent of Sister Kenny. She should be given credit for having the idea accepted, but equal credit is due the National Foundation for Infantile Paralysis, Inc., for giving her the opportunity to demonstrate her ideas. Without its aid, she too would not have been heard.

It is not certain whether Sister Kenny gets good results because of the meticulous application of good

reeducational principles or because of the hot compresses which she insists on using. My deduction would be that reeducation is the chief reason. Her statement that this type of heat is better than any other is something that must also be checked. Sister Kenny herself probably realizes that her work has to be verified.

One wonders why the authors introduce such bizarre ideas of physiology in order to explain certain functions that could be explained simply, without straining the imagination and without the introduction of such complex terms as mental alienation, incoordination and spasm. The fact that these physiologic beliefs have not been accepted does not in any way detract from the usefulness of Sister Kenny's regimen.

There are things about Sister Kenny's dictums that can be questioned. Her concept of pain, spasm and the cause of spasm does not seem to fit the facts. However, it must be admitted that there is progress outlined in this volume. It is a good book, although not a classic. Much that has been written cannot be concurred with, but pediatricians treating this disease can read the book with great benefit.

Directory of Pediatric Societies *

INTERNATIONAL

INTERNATIONAL ASSOCIATION OF PREVENTIVE PEDIATRICS

President: Prof. S. Monrad, Dronning Louises Børne-hospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

INTERNATIONAL CONGRESS OF PEDIATRICS

President: Dr. Henry F. Helmholtz, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Charles F. McKhann, University Hospital, Ann Arbor, Mich.

Canadian Committee:

Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston. Time: Postponed indefinitely.

INTERNATIONAL CONGRESS FOR THE PROTECTION OF INFANCY

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

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General Secretary: Dr. Alfredo Largaia, Cerrito 1179, Buenos Aires.

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NEDERLANDISCHE VEREEN GING VOOR KINDER-GENEESKUNDE

President: Dr. J. H. G. Carstens, Servaasbolwerk 14^a, Utrecht.
Secretary: Dr. R. P. van de Kastele, Laan van Poot 340, 's Gravenhage.
Place: Different places. Time: Three times a year.

PAEDIATRICKÝ SPOLOK NA SLOVENSKU

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialkstr., Tel Aviv.
Secretary: Dr. A. Brunn, 9 Maazestre, Tel Aviv.

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President: Dr. Angel A. Aballí Arellano, 17 No. 609 Vedado, Habana.
Secretary: Dr. Julio G. Cabrera Calderin, Hospital Mercedes L y 21 (Vedado), Box 2430, Habana.
Place: Cátedra de Clínica Infantil, Hospital Mercédes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Fernando López Clares, 12/a. Medellín 191, Mexico.
Secretary: Dr. Jesus Gómez Pagola, Versalles 64, Mexico.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. E. Santos Mendoza.
Secretary: Dr. P. Oropeza, Hospital de Niños, Caracas.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weil-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Halé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sévres.
Time: 4:30 p. m., third Thursday of every month.

URUGUAYAN SOCIETY OF PEDIATRICS

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Secretary: Dr. Alfredo Ramon Guerra, Paysandú 824, Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

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Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.

AMERICAN ACADEMY OF PEDIATRICS

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Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S
HOSPITAL SECTION

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AMERICAN PEDIATRIC SOCIETY

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CANADIAN SOCIETY FOR THE STUDY OF DISEASES
OF CHILDREN

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SOCIETY FOR PEDIATRIC RESEARCH

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Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

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Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Warren R. Sisson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. C. G. Ashley, 833 S. W. 11th Ave., Portland, Ore.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. Arild E. Hansen, University of Minnesota, Minneapolis.
Secretary-Treasurer: Dr. Albert V. Stoesser, 205 W. University Hospital, Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

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Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver.

SOUTHERN MEDICAL ASSOCIATION, SECTION
OF PEDIATRICS

Chairman: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.
Secretary: Dr. Angus McBryde, 604 W. Chapel Hill St., Durham, N. C.

STATE

ALABAMA PEDIATRIC SOCIETY

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Secretary-Treasurer: Dr. Ruth Berrey, 2021-6th Ave. N., Birmingham.

ARIZONA PEDIATRIC SOCIETY

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Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

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ON PEDIATRICS

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Secretary: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Ludo Von Meysenbug, Box 3356, Daytona Beach.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. T. F. Davenport, 104 Ponce de Leon Ave. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB
OF CONNECTICUT

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Time: Three meetings a year.

ILLINOIS STATE MEDICAL SOCIETY, SECTION
ON PEDIATRICS

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

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President: Dr. K. T. Knobe, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

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NEBRASKA PEDIATRIC SOCIETY

President: Dr. E. W. Hancock, 820 Sharp Bldg., Lincoln.

Secretary-Treasurer: Dr. John M. Thomas, 1102 Medical Arts Bldg., Omaha.

Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. MacLean J. Gill, 14 N. State St., Concord.

Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.

Time: Twice yearly.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Arthur H. London, 1105 W. Main St., Durham.

Secretary: Dr. Jay M. Arena, 604 W. Chapel Hill St., Durham.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Ben H. Nicholson, 301 N. W. 12th St., Oklahoma City.

Secretary: Dr. Luvern Hays, 168 W. 6th St., Tulsa.

Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Lonita Boggs, 361 E. Coffee St., Greenville.

Secretary-Treasurer: Dr. Hilla Sheriff, Wade Hampton Office Bldg., Columbia.

TEXAS PEDIATRIC SOCIETY

President: Dr. F. H. Lancaster, 4409 Fannin St., Houston.

Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Edwin A. Harper, 301 Rivermont Ave., Lynchburg.

Secretary: Dr. Emily Gardner, 1100 W. Franklin St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY,
SECTION ON PEDIATRICS

President: Dr. Andrew Amick, 1021 Quarrier St., Charleston.

Secretary: Dr. A. A. Shawkey, Professional Bldg., Charleston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND
PEDIATRIC SECTION

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave., Cleveland.

Secretary: Dr. I. B. Silber, 10465 Carnegie Ave., Cleveland.

Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO,
SECTION OF PEDIATRICS

President: Dr. I. Nelles Silverthorne, 170 St. George St., Toronto, Canada.

Secretary: Dr. G. P. Hamblin, 2333 Bloor St. W., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry J. Cohen, 1975 Walton Ave., New York.

Secretary: Dr. Walter Levy, 12 E. 88th St., New York.

Place: Concourse Plaza Hotel, 161st St., and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Harry A. Naumer, 37-8th Ave., Brooklyn.

Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.

Place: Granada Hotel. Time: Fourth Wednesday of

October, November, February, March and April.

BUFFALO PEDIATRIC SOCIETY

President: Dr. A. Wilmot Jacobsen, 187 Bryant St., Buffalo N. Y.

Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo, N. Y.

Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Edward J. Wynkoop, 501 James St., Syracuse.

Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.

Places: Various cities in New York. Time: Third Tuesday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Heyworth N. Sanford, 952 N. Michigan Ave., Chicago.

Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago.

Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

CINCINNATI PEDIATRIC SOCIETY

Secretary: Dr. T. Selkirk, 3530 Reading Rd., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati.
Time: On call.
President: Dr. Lloyd K. Felter, 3144 Jefferson Ave., Cincinnati.

DALLAS PEDIATRIC SOCIETY

President: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas, Texas.
Secretary-Treasurer: Dr. Gladys J. Fashena, 4585 Bel-
fort, Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second
and fourth Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. Hugh Lewis, Detroit, Mich.
Secretary: Dr. John J. Pollack, 622-26 Maccabees Bldg.,
Detroit, Mich.
Place: Wayne County Medical Society. Time: 8:30
p. m., first Wednesday of each month from October
to June, inclusive.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRICS
SECTION (ATLANTA, GA.)

Chairman: Dr. Don F. Cathcart, 478 Peachtree St.
N. E., Atlanta.
Secretary: Dr. Harry Lange, 478 Peachtree St., N. E.,
Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E.
Time: Second Thursday of each month from October
to April, 8 p. m.

HOUSTON PEDIATRIC SOCIETY

President: Dr. Raymond Cohen, 2300 Caroline St.,
Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd.,
Houston, Texas.
Place: College Inn, Houston. Time: Fourth Monday
of each month.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Edwin H. Schorer, 1103 Grand Ave.,
Kansas City.
Secretary: Dr. H. E. Petersen, Kirkpatrick Bldg., St.
Joseph, Mo.
Place: Kansas City General Hospital. Time: On call.

LOS ANGELES COUNTY MEDICAL ASSOCIATION,
PEDIATRIC SECTION

President: Dr. Oscar Reiss, 2200 W. 3d St., Los
Angeles.
Secretary-Treasurer: Dr. Elena Boder, 1830½ Lucille
Ave., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925
Wilshire Blvd. Time: Second Monday of February,
April, June, October and December.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND
THE ACADEMY OF MEDICINE OF BROOKLYN,
PEDIATRIC SECTION

President: Dr. Abraham M. Litvak, 1145 Eastern Park-
way, Brooklyn.
Secretary: Dr. Harold Levy, 750 St. Marks Ave.,
Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m.,
fourth Monday of each month, October to April,
inclusive.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC.,
SECTION ON PEDIATRICS

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens
Village, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th
Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills,
N. Y. Time: Third Monday of October, January,
March and May.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA,
SECTION ON PEDIATRICS

President: Dr. Harry A. Spigel, 2647 Connecticut Ave.,
Washington, D. C.
Secretary-Treasurer: Dr. Perry W. Gard, 2520 Wood-
ley Rd., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time:
8 p. m., fourth Thursday of every month.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. F. T. Mitchell, 376 S. Bellevue Ave.,
Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madi-
son Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. John H. Reynolds, 1628 W. Wisconsin
Ave., Milwaukee.
Secretary-Treasurer: Dr. F. J. Mellencamp, 324 E.
Wisconsin Ave., Milwaukee.
Place: Milwaukee Athletic Club. Time: Second Wednes-
day of each alternate month, beginning with February.

NEW YORK ACADEMY OF MEDICINE, SECTION
OF PEDIATRICS

Chairman: Dr. Howard Craig, 175 E. 79th St., New
York.
Secretary: Dr. Alfred E. Fischer, 73 E. 90th St., New
York.
Place: New York Academy of Medicine, 2 E. 103d St.
Time: Second Thursday of each month from October
to May, inclusive, 8:30 p. m.

NORTHERN CALIFORNIA AFFILIATES

President: Dr. Crawford Bost, 400 Post St., San
Francisco.
Secretary: Dr. William A. Reilly, 384 Post St., San
Francisco.
Time: Second Thursday of September, November,
January, March and May.

OKLAHOMA CITY PEDIATRIC SOCIETY

President: Dr. William M. Taylor, 1200 N. Walker
St., Oklahoma City.
Secretary: Dr. G. R. Felts, 625 N. W. 10th St., Okla-
homa City.
Place: Oklahoma Club. Time: Third Thursday of
each month.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Carl Fischer, Greene and Coulter Sts.,
Germantown, Philadelphia.
Secretary: Dr. Sherman Little, 1740 Bainbridge St.,
Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time:
Second Tuesday in January, March, May and
November.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown, Pa.

Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh.

Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Stanley Meade, 913 Floyd Ave., Richmond, Va.

Secretary-Treasurer: Dr. Louise Galvin, 214 S. Boulevard, Richmond, Va.

Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Herbert Soule, 122 Rutgers St., Rochester, N. Y.

Secretary-Treasurer: Dr. Jerome Glaser, 300 S. Goodman St., Rochester, N. Y.

Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Jerome Diamond, 503 N. Grand Ave., St. Louis.

Secretary-Treasurer: Dr. Mary A. McLoon, 408 Humboldt Bldg., St. Louis.

Place: St. Louis Medical Society Bldg. Time: First Friday of each month from November to June.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Frederick B. Joy, Stimson Bldg., Seattle.
Secretary: Dr. Sherod M. Billington, Medical Dental Bldg., Seattle.

Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.

Secretary: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.

Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Campbell Harvey, 35 W. Huron St., Pontiac, Mich.

Secretary: Dr. Harry A. Towsley, University of Michigan, Department of Pediatrics and Communicable Diseases, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRICS SECTION (NEW YORK)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.

Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.

Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.

CLINICAL ADEQUACY OF A SINGLE MEASUREMENT OF VITAMIN A ABSORPTION

EDWARD L. PRATT, M.D., AND KATHLEEN R. FAHEY, A.B.

BOSTON

The measurement of the rate of absorption of vitamin A has proved to be of value in the study of patients with chronic disturbances of nutrition. Empirically it has been found to be useful in the study of these patients, even though it may be influenced by several factors besides the intestinal absorption of fat.¹ However, the time consumed in making the numerous determinations and the difficulty in obtaining several consecutive samples of venous blood from small infants has limited the usefulness of the test.

The following study, based on the curves for the rate of absorption of vitamin A for 112 patients, aged 4 weeks to 12 years, was made in order to determine the feasibility of simplifying the procedure. This study reveals that for patients in this particular age group a single determination of vitamin A and carotenoids in the blood made at an appropriate interval after administration of the test dose provides information of the same clinical value as that obtained from more frequent determinations.

Detection of the etiologic factors producing a nutritional disturbance is essential for competent treatment. Parenteral and enteral infections, congenital anomalies, pancreatic fibrosis, true celiac disease and numerous less common disorders must be considered. Absorption of vitamin A has been shown to be low in persons with pancreatic fibrosis and celiac disease.² However, this condition is not diagnostic of these diseases, since a low rate of absorption is found in persons with other related diseases.^{2c}

From the Department of Pediatrics, Harvard Medical School, and the Infants' and Children's Hospital.

1. Josephs, H. W.: Studies on Vitamin A: Vitamin A and Total Lipid of the Serum in Pneumonia, *Am. J. Dis. Child.* **65**:712 (May) 1943.

2. (a) Chesney, J., and McCoord, A. B.: Vitamin A of Serum Following Administration of Haliver Oil in Normal Children and in Chronic Steatorrhea, *Proc. Soc. Exper. Biol. & Med.* **31**:887, 1934. (b) Blackfan, K. D., and May, C. D.: Inspissation of Secretion, Dilatation of the Ducts and Acini, Atrophy and Fibrosis of the Pancreas in Infants, *J. Pediat.* **13**:627, 1938. (c) May, C. D., and McCreary, J. F.: The Absorption of Vitamin A in Celiac Disease: Interpretation of the

The true value of the measurement of the absorption of vitamin A in the study of patients with chronic nutritional disturbances is that the finding of a normal rate of absorption practically eliminates the diagnoses of pancreatic fibrosis and celiac disease, whereas a low rate indicates the necessity for determining the enzymatic activity of the duodenal contents if one is to make an early diagnosis of pancreatic fibrosis. Since early intensive treatment offers considerable hope for patients with this disease,³ any simplification of the steps by which the diagnosis can be reached will be of value. Also, a means of eliminating quickly and simply the possible diagnoses of pancreatic fibrosis on celiac disease for many patients with chronic nutritional disturbances would be of inestimable help to physicians and would reassure the parents of the patients.

METHODS AND RESULTS

Of the 112 tests studied for this report, 38 were made for patients with pancreatic fibrosis, as proved by clinical, roentgen and laboratory examinations, including a satisfactory enzymatic analysis of the duodenal contents, and by their clinical courses. In most instances there was a subsequent postmortem examination which verified the diagnosis. The remaining 74 tests were taken from consecutive records in the files of the laboratory. The only criterion for selection was that the fasting level of vitamin A and of carotenoids and the three hour and five hour postabsorptive levels of vitamin A had been determined. In numerous instances seven hour levels also were available.

Of the 112 patients, 15 were under 3 months of age, 22 between 3 and 6 months, 23 were between 6 months

Vitamin A Absorption Test, *ibid.* **18**:200, 1941. (d) Breese, B. E., Jr., and McCoord, A. B.: Vitamin A Absorption in Celiac Disease, *ibid.* **15**:183, 1939.

3. (a) Andersen, D. H., in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1942, vol. 1, chap. 29, sect. 2. (b) Farber, S.: Pancreatic Insufficiency in the Celiac Syndrome, *New England J. Med.* **229**:653 and 682, 1943. (c) Flax, L. J.; Barnes, M., and Reichert, J. L.: Vitamin A Absorption and Its Relation to Intestinal Motility in Fibrocytic Disease of the Pancreas, *J. Pediat.* **21**:475, 1942. (D) Rekers, P. E.; Pack, G. T., and Rhoads, C. P.: Metabolic Studies in Patients with Cancer of the Gastrointestinal Tract, *J. A. M. A.* **122**:1243 (Aug. 28) 1943.

and 1 year, 25 were between 1 and 2 years and 27 were between 2 and 12 years.

The technic employed for the measurement of the carotenoids and the vitamin A in the blood plasma and the system of units used for expressing the values for carotenoids and vitamin A were those described by May, Blackfan, McCreary and Allen.⁴

In the measurement of the rate of absorption 0.1 cc. of percomorph liver oil (approximately 60,000 U. S. P. units per gram) per pound of body weight was administered orally. Samples of blood were collected prior to and three, five and sometimes seven hours after the administration of the test dose.

In order to determine at what interval after the ingestion of the test dose the highest level of vitamin A

the five hour interval in the older groups. Only occasionally in these age groups did the peak occur more than five hours after the administration of the test dose. None of the levels obtained at the end of seven hours exceeded those obtained after five hours by such an amount as to alter the interpretation of the test, except those obtained for patients with cretinism. In 13 instances the vitamin A content of the plasma was considerably lower five hours than it was three hours after the test dose, but in only 5 instances would the lower reading have led one to conclude that the rate of absorption was decreased when actually it was normal. Thus it is found that readings taken at the end of four hours for infants under 6 months of age and at the

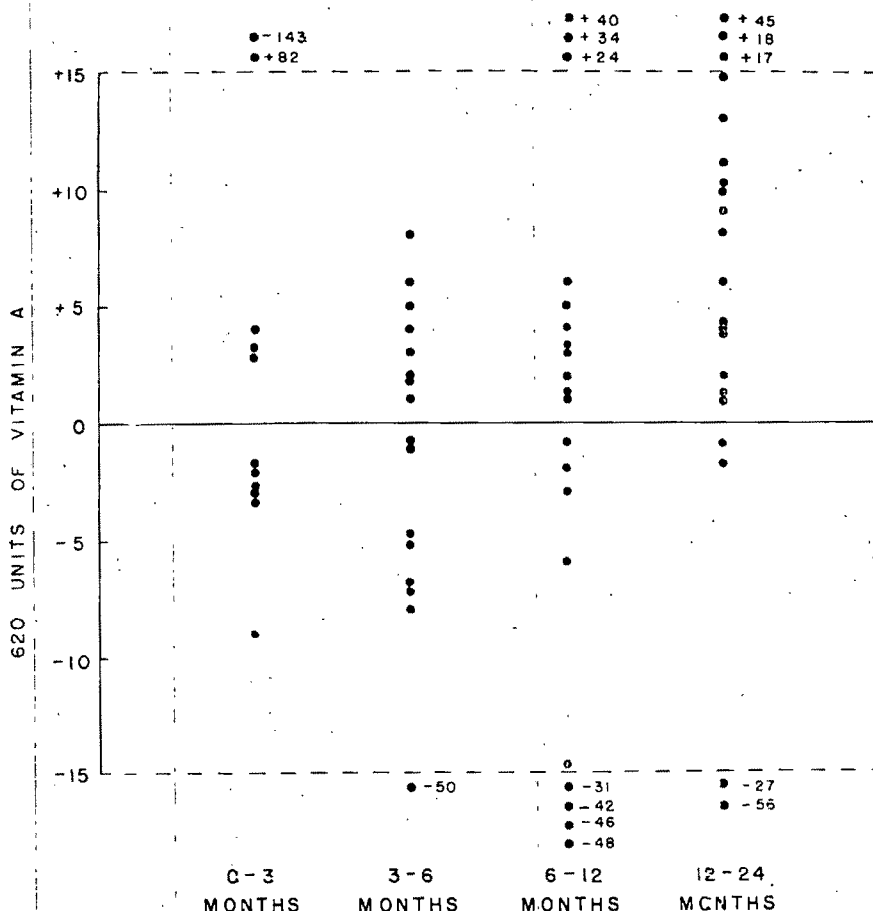


Chart 1.—The differences between the postabsorptive levels of vitamin A as measured three hours and five hours after the administration of the test dose in relation to the ages of the patients.

would be most likely to occur, the number of units that the five hour level was above or below the three hour level was charted (chart 1). The three hour level was taken as zero, and the difference between the three and five hour levels was plotted on the ordinate. These graphs demonstrate that the distribution of the highest values differed with the ages of the patients, about an equal number occurring at the end of the three and of the five hour interval in the youngest group and being confined almost entirely to

end of five hours for older infants and children would be most satisfactory.

Since the level of the plasma carotenoids does not rise during the first five hours following ingestion of percomorph liver oil,⁴ an analysis of the carotenoids in the four or five hour sample of blood defines the fasting level of carotenoids. Hence, though only one sample is taken, this information, which is of some clinical significance,^{2c} need not be sacrificed.

The fasting levels of vitamin A were studied in order to determine whether either the absolute value or the relationship of the fasting level to the highest post-absorptive level would be clinically useful in the diagnosis of the conditions present in the patients of this group. On the basis of the tests of absorption of

4. May, C. D.; Blackfan, K. D.; McCreary, J. F., and Allen, F. H., Jr.: Clinical Studies of Vitamin A in Infants and in Children, *Am. J. Dis. Child.* 59:1167 (June) 1940.

vitamin A the subjects were classified into three groups, those with good, those with moderate and those with low postabsorptive rise in vitamin A. The ranges of the fasting levels of vitamin A for the three groups overlapped considerably, and the average fasting value for the subjects with low and with moderate postabsorptive rises was practically the same, 6.0 and 7.8 L620 units respectively. Neither the difference between the peak value and the fasting value nor the quotient of the peak value divided by the fasting value proved to be of as much significance as the absolute height of the increase in the vitamin A content. Hence it would appear that determination of the fasting level of vitamin A can be eliminated without affecting the value of the test.

The distribution of the maximum postabsorptive levels of vitamin A for 38 patients with pancreatic fibrosis and 31 normal persons is shown in chart 2.

For patients with pancreatic fibrosis the level of the plasma carotenoids ranged from 0 to 10.6 L440 units, with an average value of 3.4. The highest level of vitamin A attained during a test of tolerance to vitamin A was 21.5 L620 units. For 23 patients with celiac disease, May and his associates^{2c} reported that the

would lead to a correct interpretation in 95 per cent of the cases.⁵ In every case for which the procedure would lead to a misinterpretation the error would be in not detecting the maximal rise in the level of the blood vitamin A and the inference would be that the absorption of vitamin A was impaired to a greater extent than it actually was. However, such false inferences, since they place the patient in the group for more intensive study, would not cause the clinician to make an error in judgment which might be detrimental to the patient. The elimination of two venipunctures and determinations should increase the usefulness and availability of the test of absorption of vitamin A. The simplified procedure is as follows: One tenth of a cubic centimeter of percomorph liver oil (approximately 60,000 U. S. P. units of vitamin A per gram) per pound (0.22 cc. per kilogram) of body weight is given

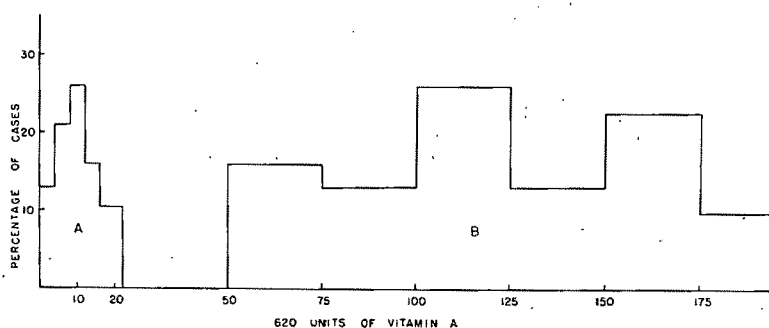


Chart 2.—Distribution of the highest postabsorptive levels of vitamin A for (A) 38 patients with pancreatic fibrosis and (B) 31 normal subjects.

range for the plasma carotenoids was from 0 to 21.5 L440 units, with an average of 6.2 L440 units and that the highest postabsorptive level of vitamin A was 37.3 L620 units. For 31 normal subjects in our series the content of carotenoids in the blood ranged from 8.2 to 103 L440 units, with an average value of 38 L440 units. The minimum postabsorptive level of vitamin A was 52 L620 units for the normal person.

COMMENT

For patients with chronic disturbances of nutrition all that one wishes to determine by measurement of the rate of absorption of vitamin A is whether this function is considerably impaired or nearly normal. Patients with impaired absorption of vitamin A deserve further study, particularly with reference to possible pancreatic fibrosis or celiac disease.

As has been shown, a single sample of blood taken four hours after the administration of a test dose of percomorph liver oil for infants under 6 months of age or five hours after the test dose for older children will enable one to determine the carotenoid content and approximately the maximal postabsorptive rise in vitamin A content. A review of each individual record in this series of 112 tests reveals that such a procedure

orally, and a single determination of the amount of carotenoids and vitamin A in the blood is made after an interval of four hours for infants under 6 months of age or after an interval of five hours for older infants and children.

CONCLUSIONS

In the differential diagnosis of chronic nutritional disturbances, the group of diseases which includes, among other conditions, pancreatic fibrosis and true celiac disease is recognized by the presence of an extensive reduction in the ability to absorb vitamin A.

Adequate evidence of significant reduction can be obtained from a single sample of blood taken at an appropriate interval after the administration of a standard dose of vitamin A.

Childrens Hospital.

5. Since the level of vitamin A was determined at only three and five hour intervals after administration of the test dose, the errors were calculated from a consideration of only the five hour level for even the youngest age group. Had a sample been taken at the end of four hours for the infants under 6 months of age it is probable that even fewer misinterpretations would have resulted.

GROUP PSYCHOTHERAPY FOR WITHDRAWN ADOLESCENTS

JOSEPH C. SOLOMON, M.D.*

Associate Chief, Department of Psychiatry, Mount Zion Hospital

AND

PEARL L. AXELROD, M.S.

SAN FRANCISCO

If one were to make the statement that a child would get along well in the world if he had been brought up in a home which afforded him a high degree of emotional security, there would hardly be a dissenting voice. It has become a well accepted doctrine that the child who has obtained all the necessary satisfactions within his own home will be able to take his place in society without any difficulty. On closer scrutiny this doctrine is only a half truth, because if the child were afforded the satisfactions of his home to the exclusion of contacts outside of the home he would be woefully unprepared for meeting the vicissitudes of a complex society. Complete emotional growth of human beings requires transitional contacts that have inherently the capacity to resemble, on the one hand, the family group and, on the other hand, the elements of conglomerate living existent in the various cultural groups to which each person must ultimately make adjustments.

Taking second thought, one becomes thoroughly cognizant of the fact that people are influenced outside of the home as well as within it. Traditionally the outside influences consist mainly of the school and the church. Each is assigned a unique responsibility for academic, moral and social teaching. The church may be looked on as the extension of the family in both the affectional and the authoritative aspects. In the school, however, the child is uniquely exposed to a fairly homogeneous age group, within which there is obtained the chance for building standards that grow out of the sharing of experiences. No matter how progressive this group experience may become, there is still an authoritative aspect to the educational setting. Education is compulsory. A voluntary group experience, on the other hand, such as is provided by playgrounds, camps, clubs and organizations like the Boy Scouts of America, takes on an entirely different complexion. The salutary effect on the development of personality of social contacts

outside of the home has, if anything, had an exaggerated emphasis in recent years. Parents have pushed the young ones out of the nest, so to speak, even from the moment of birth, with the result that the close interpersonal relationship of parent and child has dwindled to a low point.

Parents are usually motivated to get their children early in their lives to form group contacts with other children of the same age. When a family moves to a new neighborhood, the question always comes up whether there will be any children of a similar age with whom the child (or children) may play. This is indeed an important consideration. Depositing a frightened 2 year old child in a nursery school, however, is another question. One must distinguish between the parents' need to have the child learn to shift for himself and the child's need to relate himself to a group situation. The preschool child centers his need for close interpersonal relationships largely on his parents. In this relationship he feels protected, sheltered and secure. Other contacts can be made smoothly and without a feeling of frustration or fear only when he has attained a measure of emotional comfort with parents who have satisfied his basic needs. Even when these needs have been gratified, the normal 3 year old child, according to Bühler¹ and others, can maintain social contact with only two or three other children of the same age. On the surface, therefore, it seems to be thoroughly fallacious to attempt to put 3 year olds in a class of 15 or 20 children.

Probably the basis for the formation of groups is the child's fear of being left alone. Dread of loss of care and love such as arises from too early separation of the child from its mother is the basis of early infantile anxiety. This concept was elaborated in a previous publication² in which it was shown that anxiety states

1. Bühler, C.: *Testing Children's Development from Birth to School Age*, New York, Farrar & Rinehart, Inc., 1932.

2. Kasanin, J.; Solomon, J. C., and Axelrod, P.: *Extrinsic Factors in the Treatment of Anxiety States in Children*, *Am. J. Orthopsychiat.* 12:439, 1942.

* Now serving in the Army of the United States.

From the Department of Psychiatry of Mount Zion Hospital.

in children often date from as early as the age of 2 years. The most salient feature of this association, however, is the relation of the child not to the other children of the group but to the teacher, who plays the role of substitute mother. In this connection it is interesting to point out Finlay's³ observation that up to the fifth grade the major emphasis from the child's point of view is on the pupil-teacher relationship. After that the child's orientation becomes directed toward a pupil-pupil relationship, with the teacher playing a subordinate role. This change is thoroughly in keeping with other expressions of the emancipation of the child from the parental ties to form associations with people like himself or at least with others of his own age.

That a child who has had satisfaction in his home can probably form outside associations has been established. It is the point of this paper that the need for these associations can be met. In the group the child learns that other children can also be loved by parents. This is acted through by developing an understanding that they must share love with others.

Psychologists have debated for years whether there is a social instinct. Trotter⁴ spoke of human beings as possessing the herd instinct demonstrated by other animals. He stated the belief that human beings of all ages are instinctively drawn to each other by strong physiologic demands. He maintained that the formation of a group is biologically a continuation of the multicellular character of all the higher organisms. Man is a social animal through his inherent constitutional makeup according to Trotter. If one accepts the hypothesis of the existence of a herd instinct, then in accord with facts presented in this paper one must accept the existence of an instinct of precisely the opposite nature.

Inasmuch as psychoanalysis has shown that feelings of love and hate may exist side by side, a herd instinct in the human being may be counterbalanced by a "hermit" instinct which operates in the opposite direction. Human beings are not prone to seek strangers for social intercourse. Instinctively human beings seem to fear and hate each other until they know each other. This is true of individual persons, religious groups and even nations. Even when a child is assured by a familiar interested adult that he will have fun and enjoyment out of a club or camp, he may prove reluctant to enter the group unless he has at least one of his good friends with him.

The group has its function and even offers genuine intrinsic pleasure, but one cannot say that human beings reach out for it as, say, an infant reaches for the breast. In the experimental project described in the body of this paper both herd and hermit instincts may be discerned.

Just as any anxiety may be a reactivation of the fear that the child has on being separated from his mother, the pleasure derived from a group relationship may be a reactivation of pleasure that the child gets out of interpersonal relationships in his home. Freud⁵ makes this point in a somewhat different manner by saying that the group with its leaders constitutes a reduplication of the family. One can see, then, that the basis of association is not merely the formation of a herd; it is the security that rests in adequate leadership. Adults who act in groups to espouse various causes or who form crowds or mobs react to a type of parental figure in a manner which satisfies their own emotional needs. The leader can become the loving parent when all the individual persons are threatened by real or imaginary dangers. Even association with a discussion group can represent the response to a need for security when a person is uncertain as to whether his own ideas are correct.

Further proof for the opinion that the group represents a reactivation of the family can be found in the manner in which people relate themselves to the group and to the leaders. People of all ages may act out fear of or resentment to leaders when they had previously shown similar attitudes to their parents. Similarly sibling rivalries may be duplicated in inability to get along with fellow members of a group. Often such attitudes are wholly unconscious, and the equation can be established only through the medium of analysis. There are several factors to be considered in this respect: (1) the personality of the leader, (2) the professional training for group leadership and (3) the reenactment of the family drama while the process is still acutely operative. Before the presentation of the specific material at hand, it may be of value to discuss briefly each of these points.

Two variables in the relationship of members of the group to the leader are the age of the individual members and their emotional stability. It was pointed out earlier that young children react to leaders in the manner that they react to their fathers or mothers. As they grow older, their needs are not so clearly leader centered, because none of their other activities are completely parent centered. In unstable persons, how-

3. Finlay, M.: *The Classroom as a Social Group*, *Am. J. Orthopsychiat.* **11**:521, 1941.

4. Trotter, W.: *Instincts of the Herd in Peace and War*, London, T. Fisher Unwin, Ltd., 1916.

5. Freud, S.: *Group Psychology and Ego Development*, London, Instructional Psychoanalytic Press, 1922.

ever, there has not been the usual resolution of parental fixations and hostilities; hence their reaction to a group situation can be compared in many respects to that of an exceedingly young child. Such persons may be referred to as being socially immature. When older children shy away from the group, the reaction is considered a symptom of a personality disorder. If the disorder is extreme, there may result an introverted or schizoid personality. Such persons draw away from others and live in a world of fantasy. The children who were studied in this investigation were thoroughly unhappy about their withdrawal and were motivated to overcome their difficulties. One could say that the motivations represented expressions of the herd instinct were it not for the fact that the girls were similarly unhappy in other interpersonal relationships that they likewise were striving to improve. Hendrick⁶ speaks of an instinct to master. The social situation is merely one environmental challenge that the human being seeks to master. To put it in another way, the girls were not enjoying the retreat from reality; they found reality as exemplified by group relationships invitingly within reach but fraught with unknown dangers. As will be pointed out later, they all presented problems in adjustments to the members of their families.

It is already understood that parents supply both love and discipline. The love serves the purpose of satisfying the basic instinctive demands of the child, whereas the discipline represents the limits set by society on the gratification of these demands. The adequate parent is the one who can consistently pour forth a high degree of affection within the framework of a reasonable display of authority. When children grow in such an atmosphere, they possess the feeling of security that is necessary for the development of stability within themselves and of adjustment to other human beings. One would think that if a leader such as a nursery school teacher, scout master or camp counselor could offer more consistent affection and responsibility than do the parents the child would naturally gravitate to the artificial group. Such is distinctly not the case. Attempts to replace parents with professionally trained leaders failed miserably in the early stages of the Soviet experiment. Severe emotional deprivations during early childhood are not easily compensated. The answer is certainly not in the addition of added authority by getting the child out of the home into

groups but in added emphasis on close parent-child ties during early childhood.

The leader as the substitute for the parent becomes invested with the dual role of acting as the protector and as the symbol of authority. Redl⁷ developed this theme in his work. True as this may be, groups are not formed merely out of the parent-child substratum. There are several other factors which will be discussed later in the reports on cases. However, we are concerning ourselves for the moment with only this one aspect of group phenomena. It can be seen from the foregoing that when there is a need for love from the parent or when there is a need to defy parental authority or at least to test its limits the individual utilizes the relationship to the leader to work out the unsolved struggle. Obviously this attitude does not depend exclusively on the personality of the leader, but rather is related to what the leader represents. As a matter of fact, the more understanding the leadership, the greater is the likelihood that these hidden attitudes will be uncovered.

It is beyond the scope of this paper to discuss the various aspects of the question of training for group leadership. Suffice it to say that the personality and the training of the leader are both vital considerations. The members of the group rely on the leader as they do or did on their parents. Each considered his parent omnipotent, able to protect him against any danger. When instability of the parent person is manifest, a feeling of insecurity is engendered in the child. This fact was shown clearly by the reactions of children to the first blackouts of the war; adults entrusted with the care of children precipitated panic among their charges when they experienced panic reactions themselves. These observations, were reported by one of us (J. S.) in a previous communication.⁸

Much has been written in recent years about democratic and authoritarian leadership. Lewin's⁹ experiments in this field contributed greatly to the understanding of reactions of people to leadership. They showed clearly that the democratic way of life offers many advantages over both the anarchic and the autocratic. It is easy to understand how hostility is mobilized through the dictatorial form of government. Similarly, authoritative leaders can precipitate bristling resentment in persons who are reminded of similar attitudes that had been shown by their parents.

7. Redl, F.: *Group Emotion and Leadership*, *Psychiatry* 5:373, 1942.

8. Solomon, J. C.: *Reaction of Children to Blackouts*, *Am. J. Orthopsychiat.* 12:659, 1942.

9. Lewin, K.: *Patterns of Aggressive Behavior in Experimentally Created Social Climates*, *J. Social Psychol.* 10:271, 1941.

6. Hendrick, I.: *Instinct and Ego During Infancy*, *Psychoanal. Quart.* 11:33, 1942.

The resentment produced in this manner is another variable in group reaction to leadership.

People single out other persons to whom they can confide their difficulties. Every normal child has a best friend. Adults form friendships and marry companions. They may seek out ministers, social workers or psychiatrists when they have difficulties. These individual relationships may be a continuation of the role formerly vested in the parent or may compensate for lacks felt during earlier periods. Skills develop in persons in these professions out of their experience in dealing with others and out of the insights developed by supervised training. These skills permit the professional adviser to understand the limitations in the handling of individual problems. The differences in the knowledge of human behavior of various people who work with others, as well as the variation in time expended in the study of individual cases, has produced an arbitrary stratification of this type of work into so-called levels of treatment. These levels are exemplified in such disciplines as counseling, personnel work, social case work, psychotherapy and psychoanalysis. A similar situation exists in group work. The similarities and differences between individual work, as exemplified by case work, and group work have been ably discussed by Wilson.¹⁰ Briefly, psychotherapy and case work represent working with individuals in order to help them reach the group, whereas group work represents working with groups in order to reach the problems of the individual members.

Group work does not imply mere congregation. Delinquent boys join together to form a gang, but when a Father Flanagan assumes leadership, the situation takes on a different aspect. Similarly, the Tuesday night bridge club is a group, but a group of mothers who have come together at the suggestion of a social worker to discuss the problems of their children arising out of the war is something different. The distinction resolves itself into the question of leadership. The sewing circle is a group, to be sure, but it bears the same relationship to therapeutic group work as the conversation of two neighbors over the back fence bears to psychotherapy.

We can distinguish at least four levels of group work. The most superficial consists of activities commonly characterized as recreation and as "education." This brings up the question whether group work is therapy or pedagogy. The argument has been smoldering for a generation with the odds swinging now in the direction of therapy. With regard to the position of group work on

the superficial level, there seems to be little reason to argue. It seems to be generally true that persons with predominantly educational backgrounds have little training in the emotional connotations of group work. The trend seems to be toward incorporation of training in group work in schools of social service rather than in teachers' colleges, but this may be true only for training in the deeper levels of group work which will be mentioned presently. It remains a sad commentary on organized education that teachers, who should be experts in child behavior, are almost uniformly unsuccessful as camp counselors.

In group work on the superficial level, the major focus of the persons comprising the group is on the activity. Whether the activity is a baseball game, a trip to the zoo or a geography lesson, it is the central point in the relationship between leaders and members. Here the differences between the compulsory aspect of the school and the voluntary aspect of the play group become manifest. Teachers who have "a way with children" become outstanding members of their profession, even if their methods are unorthodox. Unorthodox pioneers have blazed the trails of progressive education. The newer ideas in education come closer to a common stamping ground between pedagogy and professional group work.

The next level of group work for the most part is removed from the educational scene, and in the field of recreation it is beyond the "let's play basketball" stage. It consists in a planned program in which the individual members have the opportunity to express their needs. The age level would make a decided difference in the relative roles of leader and members of the group. For small children a great degree of direction is needed, but in groups of older children more participation by the members is encouraged. Trained leaders should know the home backgrounds of their charges as much as possible. Confidential information should be held inviolate. Leaders should be prepared to confer with teachers and social workers on the needs of individual children.

The second level of group work has been most adequately described in a recent book by Cassidy and Baxter.¹¹ One of the group experiences described by these authors was the Pomo Trail Camp, in which the group was composed of students taking a course in camp counseling. One of the authors of this article (J. C. S.) was a member of the faculty of that group and had

10. Wilson, G.: *Group Work and Case Work*, Family Welfare Association of America.

11. Baxter, B., and Cassidy, R.: *Group Experience—The Democratic Way*, New York, Harper & Brothers, 1943.

occasion to participate in the program as one of the leaders. The observation of democratic and autocratic principles as a living experience proved to be both fascinatingly interesting and highly instructive. As a growth phenomenon for essentially normal persons, group work on this level offers the greatest advantages for the participants. To discuss the matter further, however, would distract attention from the essential goal of this paper, which is oriented to the handling of unstable persons.

The third level of group work can be termed social group work. It corresponds in group work to case work or superficial psychotherapy in individual therapy. It requires highly skilled workers who have the capacity for dealing with difficult problems. The groups should be small, and the program should be completely oriented to the needs of the individual participants. The family background and historical past of each member of the group should be known to the leader. Records should be kept of all the activities of the group as well as records of each member. Opportunity should be afforded for consultation with trained supervisors. The group leaders should be active participants in all conferences with social agencies and psychiatrists who are helping to determine the destiny of any member of the group. This type of work may be carried in movable groups such as those organized through the community center, the juvenile court or social agencies, or in resident groups, such as those in institutions for the care and treatment of delinquent adolescents. It is generally understood that some type of improvement in social adjustment will take place through participation in a well organized group with highly trained direction.

The fourth level of group work is that termed group therapy or, more exactly, group psychotherapy. It must be clearly understood that this delineation of levels is purely descriptive and not a clear demarcation. In the light of other work in group treatment some investigators may question whether the experiment reported in this presentation actually belongs to this fourth level of group work or conforms more nearly to what was described as the third level, or social group work. The answer to this purely academic question may be obtained by reviewing briefly some of the literature on group therapy.

The need for group therapeutic methods has arisen from the fact that individual psychotherapy is not always available for the large numbers of persons who might profit by its use. This is both an economic issue and one which is based on the number of available psychiatrists who can

devote themselves to the time-consuming processes of modifying human behavior through the individualistic approach. In addition, and perhaps more important from the point of view of research, group psychotherapy has certain intrinsic powers for therapeutic success that do not exist in individual therapy.

For the most comprehensive review of the recent literature on group psychotherapy the reader is referred to an article by Thomas.¹² He highlights some of the major concepts of the subject. Thomas follows the suggestion of Moore¹³ that psychotherapeutic methods are of two types, (a) repressive-inspirational and (b) analytic. We think that there is some question whether the methods that are described as repressive-inspirational should be called psychotherapeutic. For the most part they are pedagogic, somewhat authoritative and distinctly directional in nature. They seem to fit more clearly into what has been described here as the first level of group work. It may be said, too, that the fact that because a group is led by a psychiatrist certainly does not necessarily mean that group therapy, in the sense implied by the fourth level of group work, is in operation. Merely giving a series of lectures to a group of neurotic persons still constitutes pedagogy. However, when the problems of human beings are discussed, and particularly when there is an opportunity for group participation, the therapeutic possibilities increase.

Various methods are employed by different workers in the field of group psychotherapy. The English psychiatrists have been highly successful in handling war neuroses by group methods. The work of Snowden,¹⁴ Maclay and Whitby,¹⁵ Blair¹⁶ and Jones¹⁷ is worthy of note. The work of Harris,¹⁸ Pratt,¹⁹ Rhoades²⁰ and Buck²¹ at

12. Thomas, G. W.: Group Psychotherapy: A Review of the Recent Literature *Psychosom. Med.* **5**:166, 1943.

13. Moore, M.: The Practice of Psychiatry, Harvard M. Alumni Bull. **16**:53, 1942.

14. Snowden, E. N.: Mass Psychotherapy, *Lancet* **2**:769, 1940.

15. Maclay, W. S., and Whitby, J.: In-Patient Treatment of Civilian Neurotic Casualties, *Brit. M. J.* **2**:449, 1942.

16. Blair, D.: Group Psychotherapy for War Neuroses, *Lancet* **1**:204, 1942.

17. Jones, M.: Group Psychotherapy, *Brit. M. J.* **2**:276, 1942.

18. Harris, H. I.: Efficient Psychotherapy for the Large Outpatient Clinic, *New England J. Med.* **221**:1, 1939.

19. Pratt, J. H.: The Principles of Class Treatment and Their Application to Various Chronic Diseases, *Hosp. Social Serv.* **6**:401, 1922.

the Boston Dispensary is engaging. Although the clinic is referred to as the "thought control clinic," the methods seem to be much more paternalistic than repressive. Marsh,²² Lazelle²³ and Wender,²⁴ working with psychotic patients, but each with a different method of approach, seem to have attained some satisfactory results. Of special interest is the work of Moreno²⁵ in the psychodrama. The spontaneously staged drama described in the course of the experiment presented in this paper is typical of the work which Moreno encourages in his unique form of group psychotherapy.

All of the methods of group psychotherapy have a few elements in common. First, there is leadership; secondly, there is a homogeneous group of persons with approximately the same problems, and, thirdly, there is regularity and continuity. In addition to these, Schilder²⁶ employed psychoanalytic interpretation and aeration of emotionally charged material. The latter approach has been used by the Oxford group, Alcoholics Anonymous and spiritual meetings, in an atmosphere of religious fervor that can be both protective and repressing. In the Schilder type of therapy, it is interpretative and educational. In dealing with neurotic patients material of the most intimate nature is brought before the group and made a subject for general discussion. Similarly, the interactions within the group are discussed openly. A member showing hostility to another member, for example, receives the open interpretation that he is showing sibling rivalry if such is indicated by his history. The reaction of one person may lead to a general discussion with all members participating.

It will be noted from reading the protocol in this report that interpretations of a too revealing nature were not made to the whole group, but rather in personal interviews and conversations.

Full knowledge of the background and thinking of the participants must be had by the leader of the group. The manner in which this knowledge is handled depends, of course, on the skill of the therapist, just as it does in individual therapy.

A few workers in the field of child behavior have made interesting contributions in the field of group psychotherapy for children. Most noteworthy in this respect is the work of Bender and Woltman,²⁷ Slavson²⁸ and Svendsen and Spiker.²⁹ Bender has made engaging use of the puppet show as a medium for the release of group emotions. She has also worked with adolescents in groups. Slavson and Svendsen have also worked with children. The work of the former is characterized by a highly permissive atmosphere in the presence of the most violent aggressions. What is lacking in the presentations of this and other work in group therapy is a critical evaluation in the light of statistical analysis. An example of good thinking in this field with inadequate validation is the excellent contribution of Spiker³⁰ at the symposium on group therapy at the 1942 meeting of the American Orthopsychiatric Association. The accusation is one which academic psychologists have hurled at psychiatrists and social workers. MacFarlane³¹ brings this point clearly into focus.

The need for new ideas for the treatment of maladjusted adolescents grows out of two salient facts, namely that persons of this age are difficult to reach and that there are an insufficient number of trained leaders who are capable of offering useful treatment. Concerning the latter point little need be said. As clinics and social agencies are depleted by the war, the problem becomes all the more acute. That adolescents do not relate themselves well to the individualized approach is also well known. They are too old to relate themselves quickly to adults as substitute parents and too young to see the need for help with their problems. The experiment reported in this presentation was an outgrowth of the awareness of these needs. Our efforts were

20. Rhoades, W.: Group Training in Thought Control for Relieving Nervous Disorders, *Ment. Hyg.* **19**: 373, 1935.

21. Buck, R. W.: Class Method in Treatment of Essential Hypertension, *Ann. Int. Med.* **11**:514, 1937.

22. Marsh, L. C.: Group Treatment of Psychoses by Psychological Equivalent of the Revival, *Ment. Hyg.* **15**:328, 1931.

23. Lazelle, E. W.: Group Psychic Treatment of Dementia Praecox by Lecture in Mental Reeducation, *U. S. Vet. Bur. M. Bull.* **6**:733, 1930.

24. Wender, L.: Group Psychotherapy: Study of Its Application, *Psychiatric Quart.* **14**:708, 1940.

25. Moreno, J. L.: Who Shall Survive? A New Approach in the Problem of Human Interrelations, Monograph 58, Washington, D. C., Nervous and Mental Disease Publishing Company, 1934.

26. Schilder, P.: Results and Problems of Group Psychotherapy in Severe Neuroses, *Ment. Hyg.* **23**:87, 1939.

27. Bender, L., and Woltman, A. G.: Use of Puppet Shows as Psychotherapeutic Method for Behavior Problems in Children, *Am. J. Orthopsychiat.* **6**:341, 1936.

28. Slavson, S. R.: An Introduction to Group Therapy, New York, Commonwealth Fund, 1943.

29. Svendsen, M., and Spiker, D.: An Experimental Project in the Integration of Case Work and Group Work Services for Children, Institute for Juvenile Research, Chicago, 1940.

30. Spiker, D.: Protective Groups in the Treatment of Young Children, *Am. J. Orthopsychiat.* **13**:659, 1943.

31. MacFarlane, J. W.: Problems of Validation Inherent in Projective Methods, *Am. J. Orthopsychiat.* **12**:405, 1942.

confined to a group of withdrawn adolescent girls.

EXPERIMENT IN GROUP PSYCHOTHERAPY

Our plan in this experiment was to utilize as much information as possible from the fields of psychiatry, psychology, case work and group work without bias or preconceived notions in any one direction. It was our purpose not to establish a fixed group but to utilize a group experience to help each member of the group make an adequate social adjustment in the general life situation. We were prepared to use any unorthodox method that might be necessary in order to accomplish the greatest gains for each person within the group, without giving too much concern to the structure of the group as such. Possible complications in attempting individual therapy in a group situation were anticipated. The group functioned as a living experience in interpersonal relationships rather than merely as a medium for group catharsis.

It was our object to make the group experience similar in essence to that ideally provided by the home, which is a place in which an individual is prepared for leaving it and experiencing wider relationships. When a girl wanted to leave the group, the reaction could be looked on as a growth phenomenon indicating that the needs of that person had been served. Eleven withdrawn neurotic girls who had been ineffectively treated by the Jewish Family Service Agency, an agency for family case work, were invited to be participants in the experimental group. The girls had proved resistant to individual help from social workers and had refused to accept referrals to the Mount Zion Psychiatric Clinic. They were uniformly described as being nervous, socially shy, hermit-like and unable to make friends. Their ages ranged from 13½ to 15 years.

One of us (P. A.), a case worker with experience in group work, planned and assumed leadership of the group. To have a woman for the leader seemed to be obvious from the outset. The other of us (J. C. S.) acted as psychiatric consultant. The movement of the group as well as individually significant material was discussed in conferences. There was additional technical assistance for craft work and recreation. As the study progressed, the leaders were constantly informed about home conditions by conferring with the family case workers. It was decided that the meetings should be held not in either the Jewish Family Service Agency or the Psychiatric Clinic but in the Jewish Community Center. It was hoped that if the meetings were held there the girls could readily step into the regular group activities of the center as they

became ready to do so. The group was accordingly provided with a large basement room that was devoted exclusively to this purpose. There were few furnishings in the room, but there was complete freedom for its use. On the same floor was a game room for adolescent boys and girls.

Brief résumés of the problems presented by each of the girls follow.

Jane was a confused 14 year old girl who came from an unstable home. Both parents had deserted on several occasions, and efforts had been made to place the children in foster homes. Jane was described as being negativistic, untidy, jittery and obviously unhappy. She was shy and found it difficult to relate herself to her contemporaries.

Evelyn was the oldest in a family of four. Her father had spent the last six years in a state hospital. She was a fairly attractive 15 year old girl, but she was rigid, cold and devoid of expression. She was quiet, shy, completely without friends and so defensive that it was difficult to evoke any emotional reaction. For five years several skillful workers from the Jewish Family Service Agency had tried to help this girl work out her problems and had found her unresponsive. Attempts to assist her in forming group relationships had also been unsuccessful.

Mildred was a shy, withdrawn 14 year old girl who gave the impression of being afraid. Her voice was low, almost inaudible, on the rare occasions when she attempted to talk. She was poorly dressed, untidy, even dirty and seemed to have little desire to look attractive. There was a long history of economic difficulty and a somewhat unstable situation in the home.

Corinne, 14, was characterized as being inhibited, fearful, almost obsessive in her personal habits, with an exaggerated need to comply with her parents' wishes. Both parents were more than ordinarily severe and laid stress on decorum and respect for adults. The daughter was encouraged to pursue "lady-like activities," and the mother had commented to the social worker with considerable pride that "Corinne is too good a girl to be interested in boys." Her major interests were occupations of a solitary nature, such as reading books and listening to the radio. She had no sustained friendships.

Ann, 13½ years old, was an extremely unhappy, neurotic girl. Her jittery, aggressive behavior and constant demands for attention made her unpopular. Both of her parents and her brother had been recent patients at the psychiatric clinic, but attempts to refer Ann had failed to bring any response. Two months prior to the formation of the group she had been placed in a foster home.

Judith was an attractive, friendly adolescent who was confused and insecure. Her home was chaotic, with the mother in a borderline psychotic condition and the father frequently in conflict with the law. Obvious rivalry with three more attractive sisters increased her uncertainty in meeting adolescent problems. She made a superficial adjustment to people but had no meaningful relationships.

Gerda was a 14 year old émigré who had come to this country with her parents in 1938. Her mother was committed to the state hospital in 1939, and Gerda became depressed and hostile toward all social workers. Because of this hostility it was necessary to accept her into the group without a recreational interview. She was timid, quiet and pensive and appeared to be delicate.

She was so afraid of groups that for the first few meetings she always brought another émigré girl. At school she was isolated. Corinne asked if she might bring this "lonely little foreign girl" to the group.

Rachel, a 14 year old girl, was referred to the group by the social worker because she was friendless and lonely. She was not disliked, but she was not sought out as a companion. The social worker felt that she needed assistance because she failed to respond to office interviews. The agency was unable to get information that would throw light on the girl's difficulties.

Hester was almost 16 when the group was formed. She was selected because the old records at the Jewish Family Service Agency described her as a self-conscious, timid girl who found it difficult to form social contacts. The recreational interview indicated that she was sophisticated and rather well adjusted. She was accepted for observation and dropped out after two meetings.

Sarah, who was 14 years old, was referred to the group because she was unable to establish good relationships with either individual persons or groups. She was selfish, grasping, uncooperative and aggressive toward other children, especially girls. She always managed to be the center of attention by boasting loudly and forcing her plans and ideas on the group. Since infancy Sarah had lived in an environment of familial discord with frequent separations and had witnessed physical abuse of her mother by her father. Intense rivalry between siblings in the home was reflected in the girl's relationships outside of the home.

Rhea, a 15 year old girl, presented an awkward adolescent appearance. She was tall and ill at ease and had a somewhat depressed expression. She had a history of enuresis, nutritional fads and sexual play with her brother. She was apathetic and found it difficult to take part in any activity or conversation. Although she was a member of the Community Center and had been to camp, reports from both sources indicated that she was shy, had no friends and made poor adjustments. (This behavior persisted although she had been to the same camp for at least three summers.) Separation from her brother and father and life with her stepmother no doubt contributed to the girl's insecurity and unhappiness.

It will be noted that the girls showed many similarities; all but 2 were shy, and all had poor relationships with contemporaries as well as other neurotic symptoms. The intelligence quotients ranged from 85 to 115. All the girls were in the eighth or ninth grade, and the chronologic ages were within a range of slightly over two years.

Each of the girls was given a preliminary interview by the leader of the group. She was informed that a group of girls of her age was being formed and that she was welcome to join. During the interview the leader obtained as much information as possible about the personality of the girl and her special interests and capabilities. The girls were told that the meetings were to be held at weekly intervals and would last for one hour.

For the first meeting of the group materials were provided for crafts and simple games in which the girls had previously expressed interest. There was no organized program of activities.

They could do as they pleased, and the leaders were there to assist them. All the girls referred to the group attended the first meeting, but three of the shyest arrived one-half hour late. As they entered the room, they completely avoided one another. There was no conversation. Each girl sought direction from the leader whom she had met previously. Each became absorbed in her own particular job.

At the first meeting a half hour passed before one girl spoke to another, and then only when the situation made speaking unavoidable. Each girl sat stiffly with her eyes glued to her work. When Corinne raised her head to look around and felt herself observed by a leader, she quickly dropped her eyes as though caught in the act of stealing. The only interpersonal communications were between leaders and girls. It became apparent from the beginning that the girls wanted to gain as much praise as possible for their various tasks. There was a subtle, implicit sense of competition. During the second meeting Mildred raised her eyes for an instant and asked Corinne what school she was attending. A few more daring ones, notably Sarah and Rhea, took up the subject with other members of the group. The leaders joined the conversation and gradually drew in some of the shyer girls on this innocuous subject of mutual interest to all of them.

Ann was somewhat different from the other girls. She fluttered around the room in an attempt to obtain the leader's complete attention, to the exclusion of the other girls. Sarah, too, bragged loudly to another girl about her achievements and her popularity at school.

Other than this, the general tone of the first few meetings was charged with stiffness and formality. At approximately the eighth meeting it was noted that some of the girls began to cluster about in groups of two or three. The interest still centered about individual crafts, but there was some interchange of talk. As a matter of fact, one or two of the girls felt sufficiently free to call across the table or wander about the room to borrow tools. They began to pass comments on the projects of others; a few even offered the suggestion that the objects being worked on could be used for personal adornment. It was about this time that the girls spontaneously asked for assistance on their projects from the leaders. Some wanted to come earlier and stay later. The sessions were prolonged to one and one-half hours. Rhea, Sarah and Jane then began to walk home together.

From the beginning of the project conferences were held with individual workers for mutual sharing of observations. These meetings were

utilized for cooperative planning of work with girls in the group as well as case work with their families. The need for cooperative planning arose when Corinne began to respond to the girls with greater freedom. She became friendly with Gerda, whom she had invited to her home. The case worker not only attempted to assist the mother with her own needs, but she also prepared her to accept Corinne's newly acquired freedom.

For four and a half months the girls continued to work with crafts without any indication of desire for other activities. Feeble attempts to organize made by Mildred met with no success. However, greater enthusiasm while at work was observed. The girls offered many original suggestions. The crafts were no longer merely a prop, but a means of personal satisfaction and self expression.

Several weeks later the beginning of group feeling was noticed; with it there developed a growing restlessness with the individualized tasks represented by crafts. Games that would stimulate small groups were introduced. Especially successful was an electric contact quiz game. Not only did it offer the interest of manipulating the device, but it served the purpose of bringing several of the girls together by having one girl ask the question and others offer answers. Those who did not wish to participate simply continued their handwork. Other games, such as parchesi, lotto, big business and monopoly, were introduced. The girls formed small groups. To have the entire group participate in some game was a rarity for weeks. A typical meeting found some girls working with clay, some painting or doing handcraft while others played games, particularly of the table variety. In spite of the varied activities, there was discussion and conversation between the members of the group.

After five months of these meetings the girls still sought the approval of the adults in the group, but there was noted an increasing desire for the members to make their own plans. This tendency was encouraged. The idea of having a party seemed to originate spontaneously. It was decided in a concerted fashion to plan a program that would be a surprise to the leaders. A committee was selected by the group to write and produce a play. Other committees were chosen to purchase food and prepare and serve refreshments. When the preparations were under way, Ann wanted to buy ten times the amount of food that would have been necessary. The desire was understandable to the leaders in view of her early emotional deprivations, but

it was not made a subject for discussion. The leader found it necessary to take an active supervisory role in the buying. The program, however, was entirely in the hands of the girls.

The play involved much killing and inhuman characters such as zombies. These parts were taken by the girls who were the most hostile members of the group. For instance, Sarah seemed to gain some emotional release from portraying the role of the killer. Rhea was pleased to be the punished person and realistically played the part of the corpse. Some of the girls seemed to gain vicarious pleasure from the performance although they could take no part in the action while others, like Gerda, were not sufficiently free to express any reaction. No attempts were made to interpret to the group the meaning of the portrayals in the light of the personalities and backgrounds of the girls. The material was understood by the leaders, as it had been discussed in conference.

It was interesting to note how the various activities of the girls reflected the emotional conflicts with which they were struggling. For example, Rhea was always extremely disturbed in any games involving money, such as monopoly. This anxiety was merely a duplication of the experience she had with actual money. It reflected clearly the type of life Rhea was obliged to live. She lived with a stepmother who had been separated from her father after a long period of disagreement. Rhea's father never sent any money for the support of her or of his wife but gave it grudgingly when Rhea went to beg for it. The leaders did not deal with this problem directly. Information, no matter how pertinent, that had been obtained from case workers and not from the girls themselves was not used. Only information that arose out of the group itself was utilized. A suitable opening for Rhea to discuss the subject was planned.

Ann similarly indicated her inward feelings while she played parchesi. She continually reached "home" before she had completed the preliminary steps. This mistake was repeated several times. The members of the group became impatient and insisted that she follow the rules. The reason for this behavior was apparent to the leader because she had discussed the subject of a recent placement in a foster home with the girl. When the tension between Ann's anxiety and the group's impatience mounted, the leader sought her out for individual attention. When the leader commented that she appeared confused about the placement in a foster home, Ann grasped the opportunity to discuss the matter further. She was given an appointment with

the leader at her office in the psychiatric clinic. The interview was held at a time when there was a change of workers at the placement agency and was given with their complete cooperation.

By this time some group feeling had developed and some of the girls felt free enough to bring up for general discussion problems facing adolescent girls, for example, insecurity with boys and with groups, "going steady," dates and make-up.

It was after a discussion of petting that Judith showed some indication that she wanted individual help. She had been manipulating clay for several weeks without producing anything. That she was gaining some satisfaction from the mere manipulation of the material cannot be denied. The clay seemed to be used also as a tool to reduce tension while she discussed her own problems. Her early history of difficult toilet training seemed to bear a direct relation to her present problems. The manner in which she used the material to gain contact with the leader, however, was interesting. She picked up a piece of clay, began to talk to the leader and gradually edged to the far end of the room, subtly inviting the leader to follow. Judith utilized this opportunity to discuss the question of petting on a more personal basis with the leader. For three meetings the leader spent part of the time following through some of the problems Judith wished to discuss. To all the other members of the group it appeared that she was merely getting some assistance with the work at hand. It was not until Judith had settled some of the questions that had been troubling her that she was able to produce the article she had been making, an ashtray.

After six months of weekly meetings the girls completely discarded crafts in favor of social activities. As it was drawing close to the end of the school term, plans for the summer became a general subject of discussion. Shirley suggested that it would be fun if the whole group went to camp together. The idea took root immediately, and engendered general enthusiasm. This suggestion led to others about hikes, picnics and parties. The idea of going to camp finally resulted in a two week camping experience on a small ranch. All but two of the girls stayed for the full two weeks; Sarah and Rhea joined the group for the last week.

The camp offered an added opportunity for the growth of group feeling. Although some of the girls had previously been to camp, this situation offered a decidedly unique experience in group living. It had been planned that one of the leaders go with the girls as a counselor. As this did not work out, a new leader joined the

group for four days. She was specially qualified for this sort of work. The recreational therapist was also able to join the group for four days. This afforded the camp counselor an opportunity to talk over her problems in handling the girls in the group, and the visiting leader was able to participate in the experience. It also enabled the leader to observe at first hand the girls' adjustment in the new setting.

After the girls came back from camp, they wanted to organize a club. The differences in the tempo of development of the members made the election of officers interesting, since those who had moved more rapidly took their rightful places as leaders of the group. The entire election was in the hands of the girls, and the balloting was secret. It was not surprising that Sarah was chosen as president and that other officers were chosen according to ability and popularity. Rhea became vice president, while Mildred, one of the least aggressive girls, became a capable secretary. Jane was elected treasurer. Ann showed her resentment by not returning the following week. Sarah discussed this situation with the group, and the girls confessed that Ann was defeated because she was disliked. The leaders utilized this opportunity to offer to the group some interpretation of Ann's behavior and of their reactions to her.

During the following meetings there seemed to be an entirely different atmosphere from that which had been evident a few months previously. Whereas the general attitude had formerly seemed to be that of each girl grasping some pleasure or satisfaction for herself, it was now thoroughly cooperative. The girls decided to call themselves the Friendship Club. They chose brown and green as their colors. Several meetings were spent in redecorating the room and painting the furniture. Rhea and Sarah drew pictures and mottos for the walls. Several of the girls volunteered to repair the furniture. When they completed their work, they had transformed their formerly colorless surroundings; the room was now attractive.

It was suggested by Sarah that the club have an open meeting to which outsiders could be invited. Mildred asked if by outsiders she meant boys. A final decision was made to bring boys at a later date. Preparations for this meeting were made. Committees were again selected by the girls to assume complete responsibility for the plans, but they asked if they might consult the leaders. When the meeting took place, Sarah unexpectedly brought 2 boys. Surprisingly, all the girls accepted the visitors with poise. The boys were completely at ease and joined in the

fun. The mutual competition for the attention of the boys appeared friendly and gay. Only Mildred objected to singing and telling stories in the presence of boys. She was told she need not participate; however, when the time came for her part in the program, she carried it off triumphantly. Not only was this behavior in sharp contrast to her former meek and inarticulate manner, but her personal appearance was noticeably changed. She was clean and neat, although poorly dressed; also she wore heavy make-up. Her eyebrows were plucked; her nails, formerly bitten, were long and brightly colored. Her hair was elaborately curled to emphasize the dramatic change.

At this meeting 2 new members were voted into the group. One was a somewhat disturbed girl referred for membership by the Jewish Community Center. This girl had applied for membership about five months before and had been turned down by the girls. They rejected her vehemently because she was "boy-crazy." The fact that they accepted her membership at this time is an indication of the growth of the group. The other new member was a friend of Ann's.

The leaders felt that the girls were functioning as a normal group and were ready for the leadership of a recreational worker. Prior to our final decision to transfer the group, the same leader who had given the recreational interview again saw each girl in order to determine the present status of her social adjustment. Every girl now had a membership in the Jewish Community Center (three girls had been members before). All but 2 girls had several extracurricular activities at school. In addition, many of the girls were attending parties, often together. Most of the members of the group were attending dances with boys, and some had begun to double date. When the girls began to demand more evening activities and outings, we felt that it was the psychologic moment to approach them regarding the transfer of the group to a recreational worker. Although the possibility of the shift had been under discussion for some time, the last meeting was interesting. The girls indicated awareness that this had been a special project. One of the girls expressed the hope that the new leader would understand them as they felt they had been understood in this group.

The leaders discussed with the girls the progress made by the group during eight months. They themselves felt that they were ready for the next step. The president called the leader a week later to say that they had been successful in securing a leader. They were planning a party and wanted the former leaders to attend.

The progress of the girls may best be summarized by briefly describing the courses of development of 2 girls, one representing ability to utilize the group as a therapeutic agent and the other inability to move without the combined individual-group approach.

CORINNE.—At first Corinne gave the impression of being a "little old lady," in both attitude and in behavior. She was prim, meticulous, without humor and extremely compulsive. She finished all the projects started by the group, did a perfect job of each thing, measured accurately, worked carefully and cleaned up thoroughly after each meeting. Her behavior followed this pattern for the first five months. Her ability to learn quickly and to do good work was utilized to help her relate to the other girls. She became assistant to the craft leader and willingly aided those who needed special help. She was overly conscious of dirt and disorder and on one occasion spent an unhappy afternoon because she got a small spot on her slacks—slacks that she wore under pressure from the group. She had resisted adamantly at first when the group suggested wearing slacks or shorts on a picnic. She objected to doing anything that she believed to be not strictly feminine. She never mentioned boys, and she blushed furiously when the subject was brought up by other members of the group. During discussions of the subject Corinne concentrated intently on her craft as if completely divorced from what was going on. She could not join in group singing and looked uncomfortable during all group performances. These performances were original with the group and perhaps did not meet Corinne's standards of "good." Also, she was not sufficiently free to join in such activity. Any group discussion or cooperative endeavor frightened her. It seemed to us that she overcame this anxiety by watching the interaction between adults and the group. She eventually became good friends with one of the shyest girls; she was well liked by all the members of the group but never became closely associated with any of the others.

Soon much of her excessive primness began to fall away; she moved freely about the room, laughed and talked with the girls and joined in group games. Her appearance became that of an adolescent girl rather than that of a child. Moderate make-up appeared, and she chattered about clothes and hair-do's. She began to walk home with some of the girls and to plan outside activities with one or two.

Corinne's development can best be illustrated by the following incidents. After about eight months the girls decided to repaint the furniture. Corinne lent suggestions as to color and surprised every one by putting on an old shirt, sitting on the floor and painting with apparent enjoyment. Spilling a little paint on herself was unavoidable, but she took the disaster with ease. She simply asked the leader how to get the paint off and continued with the job. About this time Corinne's mother dropped by to thank one of the leaders for the assistance given the girl. She described an entirely different Corinne. She said that the girl was happy and carefree, sang around the house, entertained friends at home and went to other homes in the neighborhood. Formerly when her father teased her about boys she blushed and left the room in anger; now she smiled and replied, "Which one do you mean, Harry, Pete or Fred?"

Corinne joined a badminton class at school and took lessons in dancing at the Jewish Community Center,

where she was now a member. There were several conferences between the case worker and the leaders of the group. An important factor in assisting this girl was her intensive, excellent work with the parents, especially with the mother. She was not only helped to greater freedom herself but was prepared to accept the changes in Corinne.

Particularly for this girl crafts were an important tool, not only in helping her through tense situations but in drawing her out and offering her ego-satisfaction. Also, the permissive attitude on the part of the adults and the freedom of the members of the group offered her an experience unlike that in her home prior to the work with the mother. The ability of other girls to discuss adolescent problems openly and their interest in their personal appearance provided incentives to be more like them.

EVELYN.—Evelyn entered the group late. She found it difficult to take a deciding step. All of her behavior showed insecurity. She was aloof, gave the girls the impression of being stuck-up, verbally deprecated all of their activities and refused to participate. She clung to adults and was ingratiating; but she continued to come to the meetings of the group. She gave the impression of being dull and stupid, although previous testing indicated that her intelligence quotient was at least 100. In games involving money (monopoly) she experienced much emotional blocking. She could neither give up what she had nor bargain for more. She could conceive only of \$10, not \$1,000. For instance, when she was offered a generous price for her holdings she always insisted on receiving \$10 more. She could not add or subtract the simplest sum, nor could she participate in simple games. It was only after a long period of teaching by an adult that she was able to take part in a game like lotto.

Because of her apparent stupidity most of the girls openly made fun of her, calling her "dumb," maliciously repaying her for her snubbing attitude. After about four months as a member of the group, she attended a Jewish Community Center picnic, at which she was completely ignored by the other girls. According to the leader she finally related herself to much younger children. She refused to join the next outing.

In crafts Evelyn was fearful, and she could not be drawn into participation. Finally, after long observation and when a friendly attitude toward the leader had developed, she agreed to start something. She selected a leather belt that required only mechanical putting together and no ingenuity or imagination. The leader encouraged this project, feeling that it held no possibility of failure, only achievement and satisfaction.

The leaders were aware that before Evelyn could achieve an adjustment within the group individual assistance would be necessary. After group discussions of common adolescent problems, the girls were advised that they were welcome to come to the office for further discussion. Evelyn was finally brave enough to come with another girl. She asked to see the leader but was evidently too frightened to face her across the desk and left without an interview. A week later she returned and was able for the first time to discuss the problems that had caused her anxiety for many years. Two of her greatest problems were her father's mental illness, including the possible hereditary aspects of it, and her

confusion regarding sex. During the individual interview she seemed to gain some release; she looked brighter, appeared happier and expressed a desire to return. Unfortunately it was necessary for Evelyn to leave for camp the following week.

It is interesting that for the first time she was able to make a good adjustment at camp. Although she had been unable to do so before, she now identified herself sufficiently with the girls to participate in their activities. She began to pay a good deal of attention to her appearance, arranged her hair in various styles, joined in hikes and games and made several articles in the craft class. There were periods when she enjoyed being alone and would go off by herself, reading a book or just day-dreaming, but she did not appear unhappy. She mentioned several times, "It is good to get away from the city and not see the newspapers and just be away from it all." Her attitude was so changed that the girls accepted her, and she became popular with the entire camp.

After returning from camp Evelyn did not return to the group or the office. There is a possibility that she felt guilty about the information she had given in her individual interview. She was therefore mailed an appointment for an office interview. She came, and she looked lovely, with well applied make-up and attractive clothes. She talked enthusiastically of a birthday party she had attended and other social activities. She did not wish to return to the group because she was now 16 and felt too grown up to associate with the girls. Evelyn was really more mature physically and in her attitudes. We felt that this was a realistic objection with which we agreed, and we did not urge her return.

During this interview and the following one Evelyn continued to talk of her problems. She sought assistance with vocational planning and it was thought advisable to refer her to the worker at the Jewish Family Service Agency. Evelyn felt that she would be able to talk to the worker and indicated no traces of insecurity in the transfer. It has since been learned that she was referred to the Jewish Vocational Guidance Bureau; she kept her appointment and responded well to the service. She was also seeing the worker at the Jewish Family Service Agency in her office.

Without the group setting it is doubtful whether this girl could have been reached in a formal office interview. In the group she could observe adults and their attitude toward other girls and their interest in helping them with their problems. Her difficulties were of such a nature that release from inner tension through individual help was necessary in order to free her toward a better adjustment. It is possible that the individual interview kept her from returning to the group, but it must be kept in mind that our major interest was in assisting the individual girl rather than in building the group.

Summary of Results.—At the conclusion of the experiment the results were summarized. Eleven neurotic adolescent girls had been treated for eight months or less. These girls had all shown social maladjustment plus other neurotic manifestations. They were predominantly shy and withdrawn. It was definitely agreed that

8 of the 11 girls had made such rapid strides in emotional development that they could no longer be considered to have personality problems. The other 3 girls were only partially helped. Hannah had so many deep-seated problems that it is a wonder that she was helped at all. Her home conditions were still a source of irritation, but her relations outside the home were decidedly improved. Rachel did not seem to have been reached by the leaders or the group. The family case work was only superficial, as it was not found acceptable. Corinne made some progress, but at the conclusion of the experiment it was felt that she could have profited by further group psychotherapy. All the other girls were essentially normal adolescents with poise and outgoing manners and with no neurotic symptoms. The 2 girls who joined the group after the project was under way were not included in this report.

COMMENT

The foregoing description of the high lights of an experiment in the treatment of a group of mildly neurotic adolescent girls furnishes excellent material for a discussion of group psychotherapy. There was unquestionably a wealth of material that was not observed or recorded that could have furnished the basis for added interpretation. It was our purpose, however, to bring into relief the most noteworthy features of the progress of the group, with omission of many trivia which might only becloud the major issues.

There are many reasons why it was decided to perform the experiment with a homogeneous group. It is known by experienced group workers that in groups in which there is a wide range in age or a great difference in intelligence and interests there is apt to be a great deal of confusion. One of the reasons for homogeneous grouping is that large discrepancies in ages reactivate natural sibling rivalries.

From the descriptions of the girls it can be seen that all of them were suffering from anxiety states of various degrees. The inability to form social contacts with contemporaries was an expression of chronic fear tensions which had been the aftermath of disturbances in the sphere of interpersonal relationships within the family. Instead of defending themselves against anxiety exclusively by the formation of symptoms, the girls shied away from people most of the time.

It has been the general experience of persons who have worked with young adolescents that there is resistance to the establishment of a working relationship with an adult of the opposite

sex. This is not necessarily true in intensive psychotherapy with extremely disturbed youngsters. But by and large it can be noted that when the physiologic changes of puberty are ahead of the psychosexual development, the complication of parent-child relationships and the stirring of heterosexuality at the same time may prove too burdensome. For this reason leaders for groups of adolescents should be of the same sex as the members of the group. In addition to the fact that when there is a leader of the same sex the likelihood of stirring up feelings of sexual guilt is more remote, there is the factor of identification. Of this more will be said later.

The fact that the girls came in for personal interviews after some preparation indicated that even though they were fearful, they were definitely motivated in the direction of emotional maturity. Yet the manner in which they entered the group suggests the formation of a class at the nursery school level of emotional development. Figuratively they had to be led by the hand by their mothers. In this instance the leader who interviewed them took on a maternal role. The one or two times that these girls were seen before the first meeting served to establish a feeling of support between child and leader which afforded a measure of security in a "well-at-least-my-mamma-will-be-with-me" manner. The maternal role vested in the leader suggests the similar role assumed by the therapist during some phases of individual psychotherapy.

It can be noted from the description of the first three meetings that there was no communication between members of the group. The only interest was in the objects absorbing the work energies and in the leaders. In Freudian terms, libidinal object cathexes were centered on things and on the parental figure. The leader-child relationship suggests the early mother-child bond, whereas the intense preoccupation with crafts suggests the interest in things rather than people that is usually demonstrated during the so-called latency period.

Actually the leader-child relationship represents not merely the infantile child-mother relationship, but rather the beginning of the reversion of the oedipal ties of the child from the parent of the opposite sex to the parent of the same sex. This reversion is accomplished through the medium of identification in the normal family set-up. In the girls of our group there were delays in the orderly sequence of psychosexual growth; they had not formed normal identifications because of disturbances in their home settings. They were striving to come to terms with their formerly hated mother per-

ons but were inhibited by their own turmoil. That these hostile feelings were present could be gleaned from the negative reactions expressed to the leaders after the girls felt free enough to release their true feelings. In the early stages, however, they were too fearful to express any feelings but sought refuge in an exaggerated interest in material objects.

The interest in objects fulfilled the dual purpose of giving opportunity for the use of various meaningful mediums of expression and serving as the connecting link between the girls and the leaders. By this means the girls could obtain attention and praise from the adults. At the same time it was apparent from the start that each girl was acutely aware of the other girls. Work activities, however, served to preoccupy them to the extent that conversation and other social contacts could be avoided. On the other hand, there was afforded the opportunity for each individual girl to lose herself in the group situation and thereby to gain a measure of security. The feeling of security operated directly against the forces that produced the feelings of anxiety from which these girls were suffering.

Because of the inadequacy of the ego development of each of these girls, they were able to find satisfaction in the idealized ego vested in the leader and in that way incorporate sufficient energy to bolster their own egos. This is another way of describing the growing feeling of security that was acquired out of identification with the leader. There was probably another process of identification, that of the girls with each other. When the original desire that each of the girls might have had for the attention of the leader was replaced by mutual identification with each other's needs, there then became manifest the first evidences of group feeling. This is the main reason that group therapy is best performed with a homogeneous group. When all of the members are of the same sex and are near each other's own age, there is a greater opportunity for each person to project himself or herself into the role of the other persons in the group.

Freud makes the statement that a group is held together by the medium of love and that group actions are performed because the individuals prefer to be in harmony rather than in opposition in order to avoid the loss of love. The growth of manifestations of love, which may have represented unconscious homosexual strivings, was noted when the girls found mutual interests. This shifting of libidinal ties from objects and parents to people like oneself represents growth from the narcissistic level to a more mature form of object cathexis.

Ego strength springs from all these forces of identification. When the power to identify with others is disturbed, there is interference with normal group formation. Lander³² showed how delinquent adolescents failed to form social adjustments. He stated that as long as a person views the family and community as being hostile and frustrating he cannot possibly identify himself with others to the extent of submerging his own personal needs to the needs of the larger group. The girls in our group did not as a general rule demonstrate this type of aggressiveness but instead withdrew as if reacting to an unknown danger. When they began to feel less threatened by contact with other human beings, they were able to reach out for more secure satisfactions.

As the girls began to experience interpersonal contacts within the group, the omnipotence formerly vested in the leader began to be questioned. They made their own suggestions about crafts and used the leaders as resources rather than authorities. This feeling was exactly in cadence with the parallel emancipation from parental ties. The girls who could not thoroughly work through these feelings were so severely bound to parental figures by their ambivalence that group work was insufficient to meet their needs.

Case work with the families of the girls served in many instances to break up the vicious cycles of hostility provoking anxiety and vice versa, so that identifications could progress more expeditiously. In spite of all these efforts, movement was slow. After twenty weekly meetings the girls were still miles apart. It is interesting, however, that the girls kept coming. No doubt they were getting some satisfaction, although it was only slightly discernible from the surface.

When the interest shifted from individual activities to games, a feeling of familiarity was already beginning. One must not lose sight of the importance of the consistency of the setting which inspired the feeling of being at home. The same place, the same hour, the same girls, the same leaders week after week instilled a feeling of security in disturbed persons whose lives were so full of conflicts and inconsistencies as to be rendered socially paralytic. When the girls attained some security, they were able to express some of their repressed emotions.

The playlet that they put on certainly lifted the lid from the encased fantasy lives of the girls. No doubt every character represented something within each of the girls. Through

32. Lander, J.: The Pubertal Struggle Against the Instincts, *Am. J. Orthopsychiat.* 12:456, 1942.

acting as a group, they were able to alleviate their feeling of guilt through the dilution of their individual thoughts with those of the others. Here again their only audience was composed of the leaders, from whom they sought approval and understanding. It was in essence a "psycho-drama" spontaneously staged.

It is noteworthy that instinctively conditioned activity sought its own expression in due time. Even when there were manifestations forthcoming, the leaders did not make any group interpretations of the instinctive expressions. The meetings were always conducted on what can be considered the ego level. Even extremely meaningful ego interpretations were carefully guarded from general discussion. It is true that some group therapists are much bolder in their interpretations and hold open discussion of intimate material with the group as a whole. In this group of adolescents such activity on the part of the leaders might have proved disastrous.

It is true that in individual therapy there is a much wider range of permissibility than there is in any home situation. Nevertheless there is a limit beyond which the therapist does not permit his patient, whether adult or juvenile, to digress. It is the pattern of consistencies such as time limits and prohibitions against destroying fixed property or inflicting pain or discomfort on the therapist that gives the child a framework within which he can build up his ego. For this reason we cannot agree with those who allow a thoroughly permissive atmosphere in the group situation. The days of "everything goes" have fortunately disappeared from progressive education and should disappear from other areas as well. If the child must build a superego within his own restrictive influences, he is apt to be much more self condemnatory than if the adult sets the limits and speaks up when the bounds have been overreached. The limits were set at first by the leaders. Later, as group solidarity became manifest, the greatest part of the responsibility for discipline became the shared interest of the entire group. Actually, the subtle discipline exerted by disapproval by other members of the group became a strong socializing force. The feeling of a gradual process of weaning throughout the progress of the group can no doubt be sensed from reading the protocol.

Wilson¹⁰ emphatically expressed her opinion that leaders of groups should not single out members for individual attention. It is her opinion that if special attention is needed by any member of a group it should be given by other case workers or psychiatrists. This may

be true for the more superficial levels of group work, especially when the leader has had no training in the technics of rendering individual assistance. It was our feeling that individual interviews helped some of the girls in our group. Interviews served to bring the girls closer to the leaders. Inasmuch as the appointments were made secretly, there was little likelihood that the individualized attention could precipitate antagonisms. The interviews were held at the psychiatric clinic to establish a bridge which could serve as a starting point for intensive treatment by a social worker or a psychiatrist, should these services meet the needs of the girls at any time in the future. While the group was still in the process of crystallization, the individual interviews served the purpose of leveling off situations in which individual members had the feeling that they were not receiving a sufficient degree of attention or love from the leader. Obviously, in the group situation the leaders remained impartial and equally interested in all the girls, but the emotional tone of leader and member changed in the minds of the girls who felt the need for extra attention. Baruch³³ has similarly found that "time alone" with the teacher helps nursery school children form group contacts more easily.

From the time the group began to function as a unit, its growth proceeded almost entirely on its own power. There is little need to go into an elaborate discussion of the group process, the "group work process" or all the fanciful theories and diagrams worked out by psychologists about the forces which draw people to each other to form groups and the way in which the group mind functions.

We feel that little would have been gained if the group had been subjected to elaborate psychologic studies to determine by objective criteria the status of interpersonal relationships. It might have been interesting from the academic point of view to have drawn up "sociograms" as described by Moreno²⁵ or to have expressed the interactions of the members of the group in the mathematical formulas described by Lewin³⁴ and his associates. Our object was not primarily directed toward describing human behavior but was concentrated on redirecting disturbed relationship in a healthy direction.

33. Baruch, D. W.: Incorporation of Therapeutic Procedures as Part of the Educative Process, *Am. J. Orthopsychiat.* 12:659, 1942.

34. Lewin, K. L.; Lippit, R., and Escalona, S. K.: Studies in Topological and Vector Psychology, *Studies in Child Welfare*, Iowa City, University of Iowa, 1940, vol. 16, p. 3.

Our interest centered around the clinical observation that there was established a feeling of group loyalty and morale operating in a social unit, whereas at the beginning there were merely 11 strange, frightened adolescent girls. That all of the girls did not profit equally from the experience does not necessarily discredit the whole experiment. Certainly no harm was done to them and probably some good. Although they may not have contributed a great deal to the growth of group feeling, they did not materially hold back the other girls, whose emotional growth proceeded unchecked.

No doubt the greatest single factor in the relaxation of these girls with each other was the feeling of mutual acceptance. The leaders accepted the members and the members accepted each other. This acceptance satisfied the basic narcissistic impulses to a degree which helped the girls to move on to later stages of psychosexual maturation. Freud says that love changes people from egotists to altruists. Manifestly the girls not only evidenced altruistic feelings toward each other but later permitted themselves to think in terms of members of the opposite sex because some of their emotional barriers were dissolved.

MANAGEMENT AND PROGNOSIS OF MEGACOLON (HIRSCHSPRUNG'S DISEASE)

REVIEW OF TWENTY-FOUR CASES

K. S. GRIMSON, M.D.; H. N. VANDEGRIFT, M.D., AND H. M. DRATZ, M.D.
DURHAM, N. C.

Patients with megacolon (Hirschsprung's disease) present difficult problems of management and prognosis. Diet, enemas, laxatives and parasympathomimetic drugs have been the major medical aids. Surgical intervention, when employed, has usually consisted of colostomy, resection of the colon, sympathectomy or emergency correction of a volvulus or perforation. The medical literature is extensive and will not be reviewed. The surgical literature has been reviewed by us in a report dealing with the surgical treatment of obstinate megacolon.¹ The conclusions based on this review are that protracted medical management of obstinate megacolon carries a high mortality, that segmental resection of the colon carries some risk and may be followed by recurrence and that sympathectomy does not alter significantly the gross pathologic condition. Sympathectomy apparently facilitates medical management and, at the same time, decreases or interrupts the impulses over the pathways for visceral pain, which give early warning of impaction, pressure necrosis or volvulus. Reports of the occurrence of such pathologic conditions after sympathectomy are multiplying. Factors that may aid in selecting medical management, sympathectomy or resection of the colon for patients with megacolon will be discussed.

The causation of megacolon has not been definitely established. The gross and microscopic abnormalities encountered have been variously described. Reports dealing with the relative incidence of involvement of a portion or of all of the colon and rectum have differed. Megacolon is a relatively rare disease. The limited number of patients studied by any one observer and the difficulties encountered in following patients for long periods make accurate observation difficult. The authors therefore feel

warranted in presenting this study of a series of cases and in making suggestions, based on pathologic types encountered, that may help prognosis and treatment.

The records of all patients with megacolon seen since the opening of Duke clinic, in 1911, have been reviewed, and the present status of the patients has been determined by correspondence and by return visits. There were 24 patients for whom the diagnosis was thoroughly established. The initial observations indicate three rather distinct types of involvement of the colon, and events occurring during the period of observation and later, as determined by the follow-up studies, warranted classification of the 24 patients into three groups. The first group included 12 patients with a form and occasionally immense enlargement of the entire colon with definitely and at times immense enlargement of the rectum. The second group included 7 patients with uniform and usually immense enlargement of the entire proximal portion of the colon ending distally usually in the sigmoid region, with a normal segment of colon and a normal rectum. The third condition presents the most serious problem in management. Four patients in group 3 died conservatively. Three treated by a stage resection of the megacolon with ileocolic resection and ileocolostomy are living. The third group included 5 patients with enormous enlargement of the sigmoid flexure and the descending colon with or without some degree of involvement of the proximal portion of the colon and of the rectum. This condition is classically separated from the others and has been described in the literature as anal achalasia. The histories of the patients in these three groups are presented arranged in each group in the order of the time of the patients when first examined.

The symptoms that seem to indicate a favorable prognosis and those that are associated with a serious risk and may indicate surgical intervention are discussed in the summary. Rectal and proctoscopic examinations and repeated roentgen studies to determine whether the lower portions of the sigmoid colon and

From the Department of Surgery and the Department of Pediatrics, Duke University School of Medicine.

1. Grimson, K. S.; Vandegrift, H. N., and Dratz, H. M.: Surgery in Obstinate Megacolon: Radical One-Stage Resection and Ileosigmoidostomy, Surg., Gynec. & Obst., to be published.

ectum are normal or are involved in the dilatation are of value for both prognosis and management.

HISTORIES OF TWELVE PATIENTS WITH UNIFORM ENLARGEMENT OF THE ENTIRE COLON AND DILATED OR EASILY DILATABLE RECTUMS (GROUP 1)

CASE 1.—S. M., a Negro girl who is 21 months old at the time of this report, was admitted to the clinic at the age of 18 months. She had received dietetic treatment, enemas and mild cathartics from birth. Defecation was obtained by a great deal of straining and never occurred spontaneously. Three or four days frequently passed between movements. The abdomen was normally moderately enlarged but would occasionally distend greatly. Examination at the time of her admission to the clinic revealed a moderately enlarged, soft abdomen containing palpable, thickened, redundant loops of colon. Digital and proctoscopic examination after evacuation of the colon revealed enlargement of the rectum and of the lower portion of the sigmoid flexure. Roentgen examination after an enema of barium sulfate suspension demonstrated moderate uniform enlargement of the entire colon. The upper portion of the sigmoid flexure of the colon was redundant, and the lower portion and the rectum were dilated. Management by the use of enemas, magnesia magma, liquid petrolatum and neostigmine bromide has been effective in controlling obstipation and preventing attacks of distention during three months of observation. The colon and rectum of this patient are uniformly enlarged, and medical management has been effective. Hospitalization has not been required.

CASE 2.—H. K., a poorly nourished white boy who was 6 years old at the time of this report, was first admitted to the clinic when he was 19 months old, primarily because of thrush of five days' duration. This condition responded readily to treatment. Obstipation and gradually increasing abdominal distention had been present since birth. Enemas and laxatives were constantly employed. The mother stated that frequently large hard masses had been present in the abdomen and peristaltic waves had been visible. Examination at the time of admission revealed a protuberant abdomen. The rectum was large and atonic. Roentgen examination after an enema of barium sulfate revealed considerable dilatation of the entire colon and rectum. Decompression and daily defecations were accomplished during ten days that the patient was in the hospital by dietary treatment and by the use of liquid petrolatum, deproteinized pancreatic extract and daily enemas. The patient was discharged with a medical program employing deproteinized pancreatic extract, liquid petrolatum and daily enemas. Six weeks later he was brought to the clinic with the abdomen again considerably distended. Defecation was achieved only by the daily use of enemas. Hospitalization was advised and refused.

Inquiry four years later has revealed that the boy is living and well. Defecation has been regular, and the abdomen has been almost normal in size. This patient with a megacolon that definitely extended through the rectum had only moderately severe symptoms, and these have subsided during the last four years. The prognosis is presumably favorable, largely because of the uniform enlargement of the colon and rectum.

CASE 3.—W. C., a white boy who was admitted to the clinic at the age of 2 years and whose age at the time of this report is 6 years had increasing constipation

during the first eight months of life and received occasional enemas and suppositories. Constipation then became more severe, although occasionally brief intervals occurred during which elimination was normal. Vomiting developed during periods of severe constipation. Enemas, suppositories, an emulsion of agar in liquid petrolatum, cascara sagrada, magnesia magma and stronger cathartics had been employed. At the time the patient was admitted to the clinic the abdomen was protuberant and the rectum dilated. Roentgen examination after an enema of barium sulfate revealed moderate enlargement of the entire colon and rectum. The sigmoid segment was slightly larger than the remainder of the bowel. Diet, training in habits of defecation and the use of deproteinized pancreatic extract, liquid petrolatum and enemas were advised. Correspondence four years later has revealed that there has been considerable improvement in the condition of the patient. One serious episode of distention of the colon occurred when the boy was 4 years old. The easy outlet furnished the enlarged colon by the enlarged rectum may have facilitated the remission of symptoms.

CASE 4.—D. W., a Negro girl who is 10 years old at the time of this report, was admitted to the clinic seven



Fig. 1 (case 4).—Roentgenogram showing moderate enlargement of the entire colon and the rectum of a 4½ year old girl. Obstipation subsided spontaneously two years later and has not recurred.

years ago. Constipation had first been noticed after an episode of diarrhea that occurred when the patient was 6 months old. Laxatives had since been necessary. The abdomen became distended if defecation was not achieved during five days. Examination at the time the patient was admitted revealed a flat abdomen and an apparently normal rectum. Roentgen examination after an enema of barium sulfate revealed enlargement of the entire colon and rectum. Peristaltic efforts were sluggish. Proctoscopic examination to a distance of 7 cm. revealed no essential abnormality. The use of an emulsion of agar in liquid petrolatum, deproteinized pancreatic extract and a diet was recommended.

Eighteen months later the patient returned and was hospitalized for eight days. Obstipation had become more severe. Periods of five or six days would lapse without defecation. The obstipation was associated with

abdominal pain, nausea and vomiting. The abdomen at this time was protuberant. By roentgen examination the colon was seen to be somewhat more enlarged. A spinal anesthetic did not alter its activity. The rectum appeared dilated (fig. 1). Evacuation was accomplished by the repeated use of enemas. Proctoscopic examination to a distance of 8 inches (20 cm.) again revealed no abnormality. Additional dietary measures, enemas and laxatives were advised. A sympathectomy was considered but was not performed. Inquiry six years later has revealed that obstipation gave difficulty for two more years and then subsided. The patient is attending school regularly, and medical attention is not required.

The history of this patient demonstrates spontaneous remission, when the patient was 7 years old, of symptoms produced by a moderately large megacolon. Two roentgen examinations made before the patient was 5 years old demonstrated involvement of the rectum. The rectal enlargement was overlooked during proctoscopic examination. It seems probable that the enlargement of the lower part of the colon and the rectum to the anus facilitated evacuation and accounted for the remission of symptoms.

CASE 5.—E. J., a white boy admitted to the clinic at the age of 3 years, whose age at the time of this



Fig. 2 (case 5).—Uniform enlargement of the entire colon and the rectum of a 3 year old boy, demonstrated by oral and rectal administration of barium sulfate. Obstipation later subsided. The patient at the age of 11 years has spontaneous defecation.

report is 11 years, had been constipated since birth. Early dietary management did not prevent straining and the elimination of extremely hard stools. Constipation progressed until during the last year before the patient was admitted to the clinic masses of fecal material had been observed all along the course of the colon. Seven days occasionally lapsed between evacuations. Daily administration of liquid petrolatum and weekly enemas had been employed. At the time the patient was admitted the abdomen was not obviously enlarged. However, fragments of hard stool could be palpated along the length of the colon. Roentgen examination after rectal and oral administration of barium sulfate revealed that the colon was uniformly involved (fig. 2).

The rectum was larger than any other segment of bowel. During six days' hospitalization the colon was cleaned out by enemas. The child was discharged with instructions that careful training, diet, liquid petrolatum and occasional enemas be employed. Inquiry eight years later has revealed that he is alive and well. Spontaneous defecation occurs daily. The abdomen is not enlarged. The history of this patient also illustrates the ease with which a megacolon emptying through an enlarged rectum may be managed.

CASE 6.—S. McE., a white boy who is 6 years old at the time of this report, was admitted to the clinic at the age of 3½ years. The first intestinal evacuation was obtained on the tenth day of life by the use of enema and castor oil. Liquid petrolatum, cascara sagrada, enemas and drastic cathartics have been constantly required. Ten to fourteen days passed between intestinal evacuations. Abdominal distention and pain developed during these intervals. Normal defecation had never occurred. Examination revealed moderate distention and roentgen studies revealed that the colon was sluggish and uniformly enlarged. The dilatation included the entire sigmoid region and the rectum. The rectal dilatation was overlooked during a rectal examination. A regimen of laxatives and enemas supplemented by mecholyl bromide was advised. A follow-up examination has revealed that the boy improved for two years. Recently medical treatment was abandoned except for the use of occasional doses of liquid petrolatum. Three attacks of severe abdominal pain with distention and vomiting occurred. Rectal examination during the return visit demonstrated definite enlargement. Two quarts of barium sulfate suspension were required to fill the colon. Roentgen examination revealed moderate enlargement of the ascending transverse and descending segments of the colon, with definite involvement of the entire length of the sigmoid flexure and the rectum.

CASE 7.—H. A., a well nourished white boy whose age at the time of this report is 17 years, was first examined at the clinic eleven years ago. Abdominal

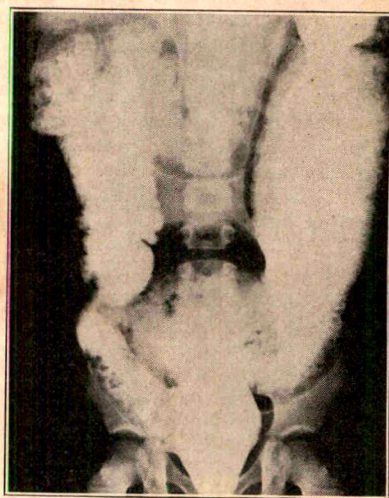


Fig. 3 (case 7).—Enlargement of the entire colon and the rectum in a 6 year old patient, demonstrated by a postevacuation roentgenogram taken after the patient had had an enema of barium sulfate. Symptoms subsided after a sympathectomy. The patient is living and well at the age of 17.

stention, severe constipation and vomiting began during the first week and continued during the first year of life. When the patient was 1 year old, the episodes of distention became periodic and could be relieved by the use of repeated enemas and castor oil. Heavy doses of liquid petrolatum later extended the intervals between attacks to four to six weeks. Shortly before the patient was admitted to the clinic, the attacks became more severe. Examination revealed a distended abdomen. Massive peristaltic movements of the colon were visible. Rectal examination revealed a large retracted rectum without palpable stool. Roentgen examination revealed enlargement and fecal impaction of the entire colon, including the sigmoid flexure and the rectum (fig. 3). The patient was hospitalized for eight days, and during that time the colon was partially evacuated. Enemas, liquid petrolatum and deproteinized pancreatic extract were prescribed. One year later he was readmitted for three days with the history that there had been little improvement. The size of the abdomen and the size of the colon and rectum as revealed by roentgen examination were somewhat greater than at the time of the previous admission. Episodes of abdominal pain and distention were recurring at intervals of two to three weeks. Inquiry ten years later has revealed that during the first two years after the last admission to the clinic the child was desperately ill several times. A sympathectomy was then performed at another hospital. The symptoms subsided, and the patient at 17 is tall, slim and athletic. In this case megacolon with involvement of the sigmoid and rectum produced serious trouble, which was apparently benefited by sympathectomy.

CASE 8.—V. H., a white girl whose age at the time of this report is 11 years, was admitted to the clinic at

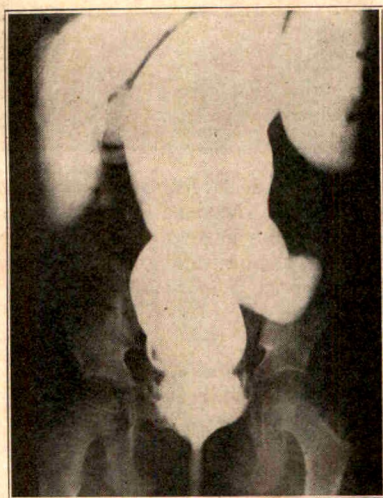


Fig. 4 (case 8).—Enlargement of the entire colon, most pronounced in the redundant sigmoid region and in the rectum, in a 7 year old girl. Medical management has effected relief of symptoms during a four year period of observation.

the age of 7 years. Constipation first developed in the patient one year after moderately severe colitis with blood and mucus in the stools. It was observed when she was $2\frac{1}{2}$ years of age and slowly became more severe. Periods of constipation and increasing abdominal distention lasted one or two months. During

the year preceding admission to the clinic the patient had normal intestinal evacuations every day for several weeks at a time, while at other times daily enemas were required. Three months before examination four weeks had passed without an intestinal evacuation. Severe abdominal pain developed. The symptoms were relieved by numerous enemas. Abdominal examination at the time the patient was admitted revealed no distention or palpable masses. The rectum was recorded as essentially normal. Roentgen examination revealed great distention of all portions of the colon. The rectum equaled in diameter the redundant sigmoid colon (fig. 4). Hospitalization was advised and refused. Medical management by the use of enemas, liquid petrolatum and diet was recommended.

A follow-up visit at the office four years later revealed that gradual improvement had occurred. Defecation occurred almost daily with the aid of liquid petrolatum taken orally and without the aid of enemas. The abdomen was somewhat full but not distended. Digital examination revealed a spacious, dilated rectum. Roentgen examination after an enema of barium sulfate revealed some enlargement of the entire colon with the greatest dilatation in the descending and sigmoid portions and in the rectum. This history also illustrates a favorable course in a patient with Hirschsprung's disease involving dilatation of the rectum.

CASE 9.—S. S., a white girl whose age at the time of this report was 16 years, was admitted to the clinic at the age of 12 years with a history of obstipation since birth. Enemas and laxatives were required for each intestinal evacuation during the first year. Voluntary movements then occurred, and enemas were necessary only occasionally. When the patient was 10 years old, a severe fecal impaction developed. She was admitted to a local hospital, where the colon was cleaned out and a diagnosis of megacolon established. Examination in the clinic two years later revealed moderate abdominal protuberance. A large mass of fecal material filled the sigmoid colon and the dilated rectum. It was thoroughly cleaned out by enemas during three weeks' hospitalization. Proctoscopic examination revealed some dilatation of the rectum and tremendous dilatation of the lower part of the sigmoid colon. Roentgen examination after injection of the colon with air, revealed some dilatation of the rectum and more dilatation of the upper part of the colon. Intestinal movements were well controlled by routine medical management and the use of deproteinized pancreatic extract. The patient was discharged. A follow-up report four years later revealed that she is now well and married. Defecation occurs without medical attention. This patient's record again illustrates the relatively benign clinical course that may develop for a patient with megacolon involving the rectum.

CASE 10.—J. W., a white man admitted to the clinic at the age of 20 years, died when he was 24. He had been moderately constipated since birth. Infrequent attacks of obstipation and moderate abdominal distention had occurred and had been relieved by medical means. The most severe attack began four weeks before he was admitted to the clinic. Defecation had become infrequent, and the abdomen had gradually increased in size. Vomiting and abdominal pain had not developed. Saline laxatives and enemas were employed without success. When the patient was admitted, his abdomen was distended by a fecal impaction that occupied the pelvis and the left side of the abdomen, extending up under the left costal margin.

Rectal examination revealed a large rectum and a long, dilated, impacted loop of sigmoid colon. The ascending, transverse and descending colon were moderately enlarged. With the patient under general anesthesia, the rectal sphincter was dilated and 4¾ pounds (2 Kg.) of fecal material was dug out of or expressed from the lower portion of the impaction. Two days later retention enemas of oil, and oral administration of liquid petrolatum and castor oil caused a mass evacuation of most of the remainder of the impaction. Liquid petrolatum, castor oil and occasional enemas then achieved daily movements. Twelve days later a moderate amount of fecal material remained. At this time the left splanchnic nerve was divided and the upper three left lumbar sympathetic ganglions were removed. The patient withstood the operative procedure well and was discharged.

Two and a half years later the patient reported that he had improved. Occasionally the bowels failed to move until liquid petrolatum was taken. Severe impactions had not recurred. The patient had married and had one child. Eight months later he called his family physician, stating that an impaction had occurred and that abdominal pain had developed. The physician reported that the abdomen was rigid, the temperature elevated and the pulse rapid and weak. Two quarts (about 1,900 cc.) of hard fecal material was removed manually through the rectum. The patient did not respond to treatment and died within eighteen hours. Autopsy revealed dilatation and impaction of the entire colon and rectum with perforation and peritonitis. The ascending colon measured 6 inches (15 cm.) and the descending colon 10 inches (25 cm.) in diameter. This history exemplifies greatly increased involvement of the colon in a patient who had a dilated sigmoid and rectum. It is possible that the sympathectomy may have adversely influenced the course of the disease by interrupting pathways for visceral pain that might have warned the patient earlier of impending trouble.

CASE 11.—M. S. was admitted to the clinic at the age of 20 years. The early history of the habits of defecation of this patient is obscure. An abscess in the right flank was drained when the patient was 11 years old. A few months later an exploratory laparotomy was performed and an angulation of an enlarged transverse colon was reduced. Constipation has since been severe and liquid petrolatum has been employed. A few months before admission the patient had adopted Christian Science. Twenty-four hours before his admission cramping abdominal pain and distention developed. Examination revealed a moderately distended abdomen. Colonic peristaltic waves were visible. There was no stool palpable in the rectum. Roentgen examination revealed a great deal of dilatation of all segments of the colon, and after an enema of barium sulfate it revealed an enlargement of the rectum and the lower part of the sigmoid colon. A complete obstruction was present in the sigmoid colon. Exploration revealed uniform dilatation and hypertrophy of the entire colon with redundancy of the ascending, transverse, descending and sigmoid segments. The lower portion of the sigmoid colon was involved in a volvulus that obstructed the colon but had not produced strangulation. The volvulus was reduced, and the appendix was removed. The patient had a satisfactory postoperative course and was discharged. A follow-up letter revealed that symptoms recurred three months later and were corrected by medical means. Although the history of the case is not complete, the evidence from its review indicates

that a true megacolon existed and that the case should be properly included in this group.

CASE 12.—W. W., a white man who was admitted to the clinic at the age of 59 years, does not remember the medical history of his infancy and childhood. Constipation necessitated frequent use of cathartics before he was 15 years old. During college years the intestinal habits became regular. For thirty years constipation and mild abdominal discomfort had been treated with various laxatives, but the abdomen had not been distended, and vomiting had not occurred. Five weeks before the patient was admitted to the clinic cramping abdominal pains developed and abdominal distention appeared. The distention increased and was not relieved by occasional defecation. Examination revealed an abdomen enlarged to approximately the size of a seven months pregnancy. Colonic peristalsis was visible. Rectal examination revealed enlargement of the rectum. Roentgen examination revealed dilatation of the entire colon, and after an enema of barium sulfate it revealed a large rectum and an incomplete obstruction near the rectosigmoid junction that was interpreted as a twist or a volvulus (fig. 5).

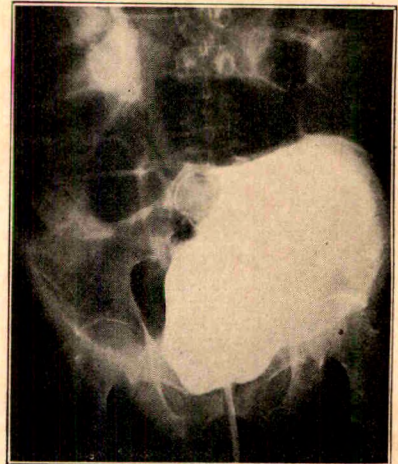


Fig. 5 (case 12).—Enlargement of the rectum and the lower portion of the sigmoid flexure and obstruction of the colon by volvulus in a 59 year old patient, demonstrated by rectal administration of barium sulfate. The megacolon produced mild symptoms before the obstruction developed.

A laparotomy was performed. The entire colon, including all of the sigmoid region and the rectosigmoid junction, was enlarged to a diameter of 6 or 7 inches (15 to 18 cm.). The sigmoid colon itself was twisted in a half turn but not strangulated. The volvulus was reduced. The postoperative course was uneventful. Three months later the patient returned with a recurrence of obstructive symptoms of nine days' duration with moderate abdominal distention. The rectum remained large. Roentgen examination again showed dilatation of the entire colon and incomplete obstruction at the rectosigmoid junction. The abdomen was explored, and a recurrence of the partial volvulus of the sigmoid colon was observed. A long segment of the large, thick, redundant sigmoid flexure was resected and continuity was restored by a lateral anastomosis. A proximal colostomy was established and later closed. This patient demonstrated uniform enlargement of the colon and rectum that gave minor symptoms until

was 59. It is possible that impaction of the proximal dilated segments will recur after the segmental resection of the colon and produce further trouble. Resection of all of the proximal colon and ileosigmoidostomy would have obviated this risk, but it was probably not indicated because of the patient's age.

HISTORIES OF SEVEN PATIENTS WITH UNIFORM ENLARGEMENT OF THE PROXIMAL PORTION OF THE COLON TERMINATING USUALLY IN THE SIGMOID REGION IN A NORMAL SEGMENT OF THE LOWER PART OF THE COLON AND A NORMAL RECTUM (GROUP 2)

CASE 13.—J. H., a white boy, was admitted to the clinic eight years ago, at the age of 10 months. He died at the age of 15 months. The history began with diarrhea, with ten to twelve stools a day, immediately after birth; the condition persisted for three weeks. Severe obstipation requiring the constant use of laxatives or enemas then developed. Vomiting also occurred persistently. A recurrence of diarrhea with blood in the stools lasting one week had taken place just before the patient was admitted to the clinic. At that time the examination revealed a distended abdomen through which peristalsis of the colon could be seen and large hard fecal masses palpated. The rectal sphincter was relaxed, and the rectum was filled with large hard feces. Roentgen examination later showed that the colon was enlarged tremendously to a point about 4 cm. above the rectum. Evacuation was accomplished by means of numerous enemas and laxatives. The child then retained all feedings and managed daily defecation with the aid of medical treatment. Distention recurred, and the child died a few weeks after leaving the hospital. The dilatation and impaction in this patient extended downward only to the lower portion of the sigmoid flexure. The normal segment of sigmoid and rectum beyond this point, although capable at times of dilating during the passage of a fecal impaction, probably facilitated the return of obstructive symptoms and contributed to the early death. A colostomy or a resection of the colon may have been indicated.

CASE 14.—W. W., a Negro boy, was admitted to the clinic seven years ago at the age of 12 months. He died at the age of 15 months. Obstipation had begun at birth, and abdominal distention was noted by the third day of life. Distention gradually progressed until the abdomen was hugely distended, with the skin overlying it tightly stretched and thin. Constant and varied medical treatment was given without effect. Vomiting recurred frequently. When the patient was admitted to the clinic, many colonic peristaltic waves were visible. The circumference of the trunk at the umbilicus was 35 inches (89 cm.). The patient was poorly developed. There was moderate respiratory embarrassment because of the abdominal distention. Rectal examination did not reveal dilatation or fecal masses. Roentgen examination revealed a gigantic colon with the cecum and the ascending, transverse and descending portions filled with feces. The rectum was of normal size. The lower portion of the sigmoid colon in several views appeared normal or only moderately dilated. There was extensive upward displacement of the diaphragm resulting in compression of the lungs and displacement of the heart transversely. The abdomen during the first week of medical treatment was reduced to a circumference of 20 inches (50 cm.). Proctoscopic examination revealed no obstruction. One week later a left lumbar sympathectomy and splanchnic-

ectomy were performed. Spontaneous defecation occurred in the hospital after the operation. Roentgen study revealed that the proximal portions of the colon were about one-half their original size but still greatly distended (fig. 6). The patient was discharged receiving dietary management supplemented by treatment with liquid petrolatum and occasionally with magnesium sulfate.

The parents brought the patient to the hospital one month later, stating that during the interval defecation had occurred every two or three days with the aid of liquid petrolatum and magnesium sulfate. The abdominal distention although variable was somewhat less than it had been before the sympathectomy. The patient had severe whooping cough. A roentgenogram revealed the colon to be tremendously enlarged and still outlined by barium given as an enema seven weeks earlier. The diaphragm remained greatly elevated by abdominal pressure. A diagnosis of pertussis was established, and the child at first responded to treatment in the hospital. Nineteen days after he was admitted, however, fulminating pneumonia developed and he died. Autopsy confirmed the diagnosis of

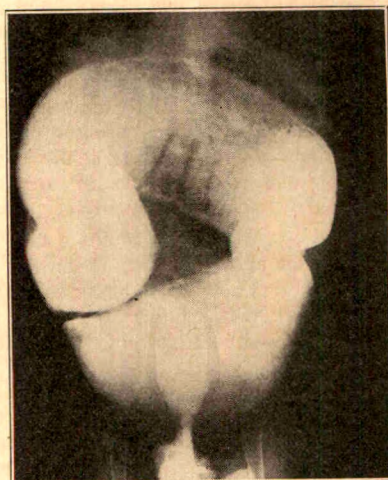


Fig. 6 (case 14).—Uniformly enlarged colon terminating in a normal lower segment of sigmoid colon and rectum in a boy 13 months old. A sympathectomy performed thirteen days before the roentgenogram was made did not improve the condition. Death occurred fifty-three days later.

terminal pneumonia. At autopsy the colon was seen to be hypertrophied and distended to a maximum circumference of $7\frac{1}{3}$ inches (18 cm.) from the cecum through the midportion of the sigmoid flexure. The lower portion of the sigmoid flexure and the rectum were normal.

The history of this case illustrates well the failure of medical management and sympathectomy to relieve obstipation and abdominal distention significantly and to prevent death from a respiratory complication in an infant with a large megacolon terminating in a normal lower section of the sigmoid flexure and rectum. Colostomy or colonic resection might have benefited this patient.

CASE 15.—The record of J. M., a white girl admitted to the clinic at the age of 2 years, has been reported in detail in a contemporary report¹ and will therefore be briefly abstracted. At the time of this re-

port she is 2½ years old. Constipation started at birth and became progressively more resistant to medical management. Abdominal distention was noted when the patient was 3 days old and progressed steadily, until, when she was 2 years old, her abdomen was enormous. Various forms of medical management at home and on several occasions in hospitals did not relieve the distention. At the time she was admitted to the clinic, the abdomen was enormously distended. The patient was poorly nourished, ate with difficulty, vomited at times and passed small amounts of liquid stool. High enemas, abdominal and rectal manipulations, liquid petrolatum, cascara sagrada, neostigmine, castor oil and duodenal intubation during three weeks in the hospital did not decompress the megacolon. The colon was uniformly involved down to approximately the junction of the upper and middle thirds of the sigmoid flexure. Below this point the sigmoid colon and the rectum were normal. A one stage resection of the distended megacolon was performed. The terminal ileum was anastomosed to the normal distal segment of sigmoid colon. The postoperative course was afebrile but was accompanied with some dilatation of the small bowel that persisted for two weeks and required intubation. Relief was finally obtained by applying a tight elastic compression bandage to the abdomen. The child was then discharged. During the succeeding three months she has maintained normal activity and gained weight. Defecation occurs three to five times daily. The stools are soft. This patient and 2 others treated by resection of the megacolon (W. H., case 17 and P. H., case 19) are the only patients in this group that are now living.

CASE 16.—R. C., a Negro boy admitted to the clinic ten years ago, at the age of 5 years, died when he was 9. Hospitalization was advised and refused. The first symptoms developed two months after birth, when several days passed without an intestinal evacuation. Castor oil effected expulsion of a large amount of fecal material and gas. Episodes of obstipation, abdominal pain and distention, anorexia and vomiting have since recurred at intervals of approximately three months. Difficulty in breathing and speaking was noted during the episodes of severe obstipation and distention. These episodes were relieved with progressively greater difficulty by catharsis and enemas. During the intervals defecation usually occurred every two days. The abdomen became chronically distended; two months before the visit to the clinic it was described as being as large as a watermelon. Enemas and cathartics achieved only small evacuations. Examination revealed a greatly distended, taut abdomen. A large colon segmented by peristaltic waves was visible. The patient was poorly nourished. The rectum was distended by a firm fecal impaction. Hospitalization was advised and refused.

Follow-up letters revealed that serious symptoms continued. When the boy was 9 years old an emergency laparotomy was performed at another hospital and a large fecal impaction was removed through an incision in the colon. The patient was discharged fifteen days later. A review of the record of this hospitalization indicates that the rectum was normal and that the impacted fecal mass was removed from the descending colon and upper part of the sigmoid flexure. Symptoms recurred and nine months later caused the death of the patient. A copy of the certificate of death gave as the immediate cause "paralytic colon" due to "obstruction due to fecal impaction." This patient

evidently falls into the group of those who are seriously handicapped by a large megacolon terminating in a normal bowel. The history of the case also illustrates that patients with this condition occasionally and with difficulty dilate the normal segments of colon and deliver fecal impactions to the anus.

CASE 17.—The record of W. H., a white boy admitted to the clinic at the age of 7 years, has been presented in detail in a contemporary report¹ and will therefore be briefly abstracted. At the time of this report the patient was 12 years old. Obstipation began at birth. Cathartics and enemas were employed continuously. Episodes of obstipation, cramping abdominal pain, acute distention and vomiting recurred. General nutrition was poor. The examination made at the time the patient was admitted revealed a greatly distended abdomen with an enormous colon, involved uniformly throughout its length, terminating in the midsigmoid region in a normal lower segment of sigmoid flexure and a normal rectum. Partial evacuation was obtained with difficulty by medical means. Three years later, at the age of 10 the patient was readmitted because of progressive

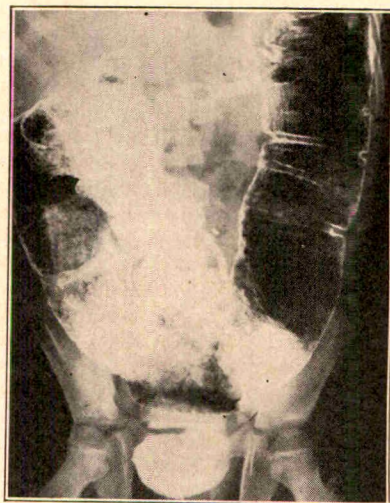


Fig. 7 (case 17).—Megacolon with normal rectum and a normal lower segment of sigmoid colon in a 10 year old patient. A sympathectomy performed fifteen days before the roentgenogram was made had partially reduced the size of the megacolon. Episodes of severe distention one year later led to a one stage resection of the megacolon.

more severe symptoms. Partial decompression was again accomplished by medical means. Sympathectomy was performed; all of the lumbar ganglia and all of the abdominal splanchnic nerves on both sides were resected. Roentgen examination fifteen days after the sympathectomy revealed reduction of the megacolon to two thirds of its original size. The rectum and the lower portion of the sigmoid colon were normal (fig. 7). For one year after this procedure defecation was more easily controlled. The state of malnutrition was unimproved. An extremely severe episode of abdominal distention and vomiting occurred when the patient was 11 and required hospitalization. The colon was again evacuated by medical means with difficulty. A one stage resection of the megacolon was performed. The terminal portion of the ileum was anastomosed to the remaining 6½ inch (16 cm.) stump of normal sigmoid

exure. The patient made an uneventful recovery and eight months later had gained 18 pounds (8.2 Kg.) above his original weight. His appearance, general nutrition and activity were normal, and soft fecal material was evacuated three to five times a day. This is the second of the 3 patients treated by one stage resection of the megacolon.

CASE 18.—E. P., a white boy admitted to the clinic at the age of 15 years, died when he was 17. Constipation, abdominal distention and vomiting had necessitated

diarrhea with evacuation of large amounts of liquid stool. Intervals as long as two to three weeks without defecation occurred every four to five months and were associated with gigantic abdominal distention, vomiting, palpitation of the heart and dyspnea. Episodes of this nature became more frequent, and the residual distention became greater. At the time the patient was admitted to the clinic the abdomen was enormously distended by large loops of colon (fig. 8A). The dilated, impacted segments rested above the pelvis and

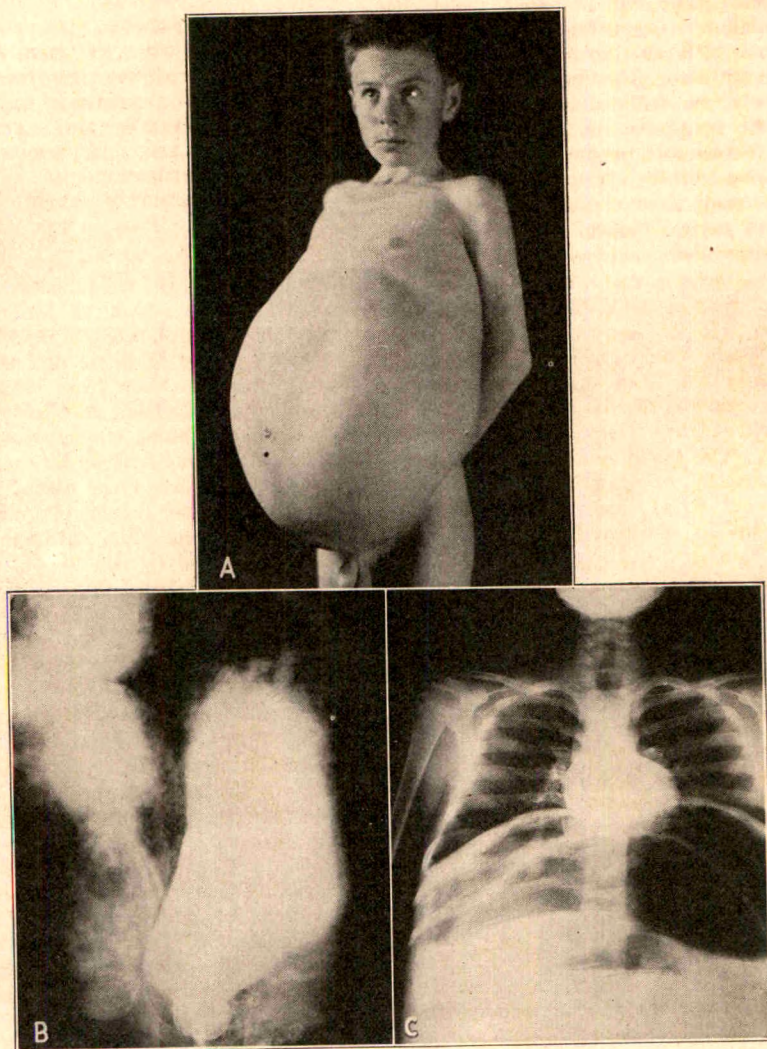


Fig. 8 (case 18).—A, photograph of a 15 year old patient with megacolon, showing the abdominal distention, which had progressed from the time of birth. The colon ruptured spontaneously two years later, and the patient died. The normal rectum and normal lower segment of sigmoid colon of this patient resisted evacuation efforts. Colon resection and iliosigmoidostomy were anatomically possible. B, roentgenogram of the same patient, showing the normal rectum and a normal lower segment of sigmoid colon. The enormously impacted loops of the proximal segments of the colon overlie the normal portion of the sigmoid flexure. C, roentgenogram of the chest showing the upward displacement of the diaphragm and the compression of the lungs in the same patient. Pulmonary and cardiac symptoms occurred during episodes of severe distention.

an enema when the boy was 9 days old. Enemas were employed daily until the patient was 6 years old. They accomplished evacuations but did not prevent progressive development of abdominal distention. Enemas were given once a week after the boy was 6. Each enema was followed by twenty-four to forty-eight hours of

could not be reached by rectal examination. Roentgen examination confirmed the clinical impression of a gigantic megacolon that involved equally all portions of the colon down to the lower part of the sigmoid flexure and the rectum (fig. 8B). The upward displacement of the diaphragm, flaring of the costal

margins, compression of the lung and transverse position of the heart are demonstrated in figure 8 C. Dyspnea and tachycardia during episodes of acute distention are understandable. High colonic irrigation, massive doses of liquid petrolatum and daily administration of deproteinized pancreatic extract achieved only moderate decompression of this colon during eleven days' hospitalization. Sympathectomy was advised and refused.

A letter of inquiry seven years later revealed that the patient had died two years after removal from the hospital. The mother stated that abdominal distention had persisted and that the obstipation had resisted all forms of surgical treatment. On the day before his death the patient had felt something break in the abdomen. The cause of death given on the death certificate was acute perforation of a megacolon and peritonitis. This record illustrates the serious prognosis that may be associated with the presence of a uniformly enlarged colon terminating in a segment of normal sigmoid colon and a normal rectum. A colostomy or a resection of the megacolon could have been performed.

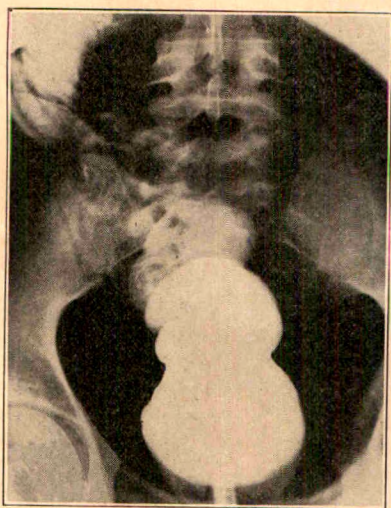


Fig. 9 (case 19).—The normal rectum, the normal lower segment of sigmoid flexure and the anastomosis between the terminal portion of the ileum and the sigmoid colon in a patient one month after resection of the megacolon. The patient was in good health one year later.

CASE 19.—The record of P. H., a white man admitted to the clinic at the age of 19 years, is presented in detail in a contemporary report¹ and will therefore be briefly abstracted. At the time of this report the patient is 22½ years old. Constipation and abdominal distention developed after birth and progressed steadily. The patient had episodes of acute impaction in late childhood. When the patient was 19, the abdomen equaled that illustrated in figure 8 A. Three hospitalizations because of distention were necessary during the next two years. The entire colon was uniformly enormous down to the lower part of the sigmoid region from which point the sigmoid colon and the rectum were of normal size. The megacolon could be evacuated by medical means only with extreme difficulty. When the patient was 21, it was evident that serious difficulty was inevitable. The megacolon was therefore resected by a one stage operative procedure, and the terminal ileum was anastomosed to the remaining short stump

of normal sigmoid flexure. The patient had a normal convalescence and during the next year gained 4 pounds (20.4 Kg.) over his initial weight. Soft fecal material is now evacuated three to four times daily. Figure 9 illustrates the short segment of normal sigmoid colon, the normal rectum and the anastomosis with the terminal part of the ileum after operation. This is the third patient treated by one stage resection of the megacolon. These 3 patients are still living at the time of this report, while the other 4 patients in this group have died.

HISTORIES OF FIVE PATIENTS WITH ENORMOUS ENLARGEMENT OF THE SIGMOID OR THE SIGMOID AND THE DESCENDING COLON WITH OR WITHOUT SOME ENLARGEMENT OF THE PROXIMAL SEGMENTS OF THE COLON, THE LOWER PART OF THE SIGMOID FLEXURE AND THE RECTUM (GROUP 3)

CASE 20.—L. B., a Negro boy, was first admitted to the clinic at the age of 6 years. At the time of this report he is 11. He was admitted to the hospital of Duke University School of Medicine twice, and in addition he was followed in the clinic for one year. Obstipation began at birth, and abdominal distention slowly increased. Four years before the patient was first admitted to the clinic an episode of acute abdominal distention and vomiting was interpreted as an intestinal obstruction and was relieved by enemas and cathartics. Two years later two weeks passed without an evacuation, and the patient became enormously distended and vomited all feedings. The patient was hospitalized, and relief was obtained by the use of enemas. Treatment since birth had included the use of a wide variety of laxatives and enemas. Another episode of obstruction, distention and vomiting lasted three days and initiated the first admission to Duke Hospital. Abdominal examination revealed enormous dilatation with intestinal patterns and fecal masses visible and palpable in all portions of the colon. Rectal examination revealed a hard fecal impaction almost at the anus. This could be pushed upward, releasing liquid feces. Roentgen examination revealed enormous dilatation and impaction of the descending and sigmoid colon and the rectum (fig. 10 A). Rectal manipulation, repeated enemas and deproteinized pancreatic extract during the next twenty days accomplished defecations but failed to evacuate the colon (fig. 10 B). One week later the abdomen was less distended and bowel movements were occurring regularly. The patient was discharged and advised to diet and use liquid petrolatum and daily enemas and to return to the clinic. Three and a half months later he was readmitted to the hospital with the history that he had gone as long as two weeks without defecation. The last movement before this admission had occurred ten days earlier. Examination revealed essentially the same conditions as were observed at the first visit. Complete evacuation of the colon was obtained within two days by high colonic irrigation. Roentgen examination after the injection of air revealed some dilatation of all segments of the colon from the cecum to and including the rectum. The patient was discharged two weeks later with a regimen of liquid petrolatum, deproteinized pancreatic extract and enemas. During the following four months defecation was regular, frequently without the use of enemas. A follow-up report three and a half years later revealed that this patient was living, although somewhat retarded. This record also demonstrates that a large megacolon associated with involve-

ment of all of the sigmoid colon and rectum may be compatible with a reasonably normal life.

CASE 21.—F. P., a white boy, was first admitted to the clinic at the age of 9 years. At the time of this report he is 20. Moderately severe obstipation and abdominal distention started at birth. Symptoms were partially controlled by laxatives. At times five or six

abdomen apparently filled by an oval mass that extended from the symphysis to the left costal margin. The rectum was of normal size. The rectum and the lower portion of the sigmoid colon seemed to pass upward behind the mass. Roentgen examination demonstrated an enormous fecal impaction in the descending colon and the upper portion of the sigmoid flexure and a relatively

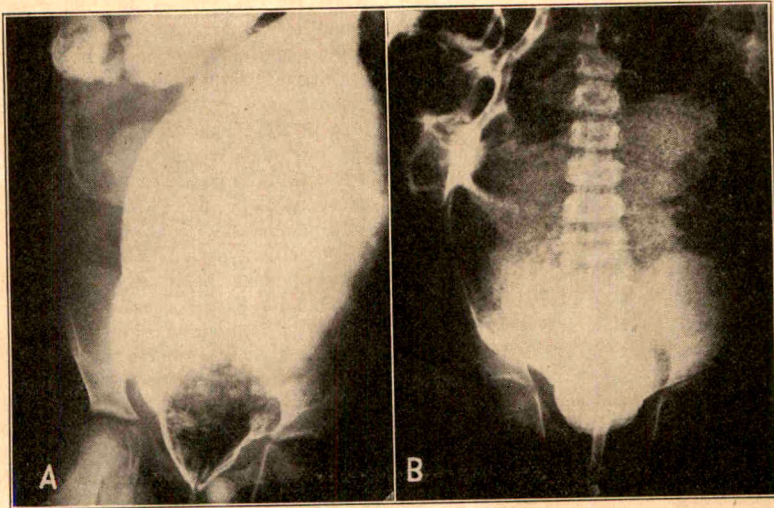


Fig. 10 (case 20).—*A*, roentgenogram showing the distended and impacted megacolon in a 6 year old boy. The major involvement is in the descending and sigmoid colon and the rectum. Rectal manipulation and medical treatment had been employed for four days. *B*, roentgenogram taken twenty days later; medical treatment has partly broken up the impaction but has not relieved the distention due to gas. This patient, with enormous involvement of the lower part of the colon and rectum, is living, without surgical intervention and with only moderate difficulty, five years later.

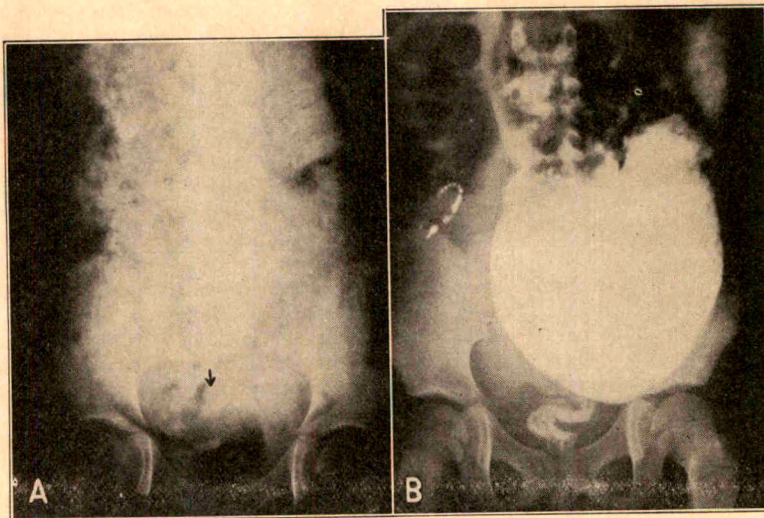


Fig. 11 (case 21).—*A*, roentgenogram showing enormously dilated descending colon and upper portion of the sigmoid colon in a 9 year old boy. The arrow indicates the normal lower segment of sigmoid colon and the normal rectum, visualized by air contrast. Additional examinations demonstrated that the proximal segments of the colon were also dilated and at times impacted. *B*, roentgenogram of the same patient showing the megacolon after repeated enemas given during nine days. The impaction has been partly washed out. The normal lower portion of sigmoid colon and rectum have not dilated.

days passed between evacuations. During the month before the patient was admitted to the hospital a hard mass became evident in the lower part of the abdomen. It was described as being about the size of a cantaloup. Defecation had occurred regularly every two or three days. Examination revealed a moderately distended

normal lower portion of the sigmoid colon and rectum (fig. 11 *A*). Manipulation, enemas and deproteinized pancreatic extract gradually cleaned out the colon. A roentgenogram taken ten days later after an enema of barium sulfate (fig. 11 *B*) demonstrates that decompression was progressing by liquefaction of the impaction

and not by dilatation of and delivery through the lower portion of the sigmoid colon and the rectum. Several weeks later proctoscopic examination and roentgen examination after an enema of air when the colon was completely empty redemonstrated a normal rectum and at least 6 inches (15 cm.) of normal sigmoid colon. The patient was discharged receiving the same program supplemented by diet and liquid petrolatum. He was followed in the clinic for twelve months. He had regular evacuations except during two episodes of impaction associated with nausea and vomiting that required many enemas. The general state of nutrition was poor. One year after his first admission to the hospital the patient was again hospitalized. The abdomen was moderately distended. The descending colon and the upper portion of the sigmoid flexure remained normal. Complete evacuation was achieved by high colonic irrigation for five days.

This boy did not return for regular observation. He did return ten years later at the age of 20 in response to follow-up correspondence. He appeared well nourished. Medical treatment during the interval consisted

lower portion of the sigmoid flexure and the rectum. The enormous capacity of the descending colon and the upper portion of the sigmoid flexure had not changed. The earlier moderate dilatation of the ascending and transverse colon had not increased.

CASE 22.—D. S., a white boy whose age at the time of this report was 16 years, was admitted to the clinic when he was 11. Abdominal distention had occurred when he was 6 months old. It was relieved by enemas. Liquid petrolatum given every other day produced regular evacuations until the patient was 5 years old. Enemas and castor oil then became necessary. De-proteinized pancreatic extract was also employed. When the boy was 9 years old, attacks of acute distention followed by massive evacuations started and recurred every two or three months. These episodes began with severe abdominal cramping pain and vomiting and ended with a period of diarrhea with frequent evacuations of thick pasty stool. An enormous amount of fecal material was usually expelled within twenty-four hours. Examination after the first admission revealed a moderately protuberant abdomen. A rounded dense

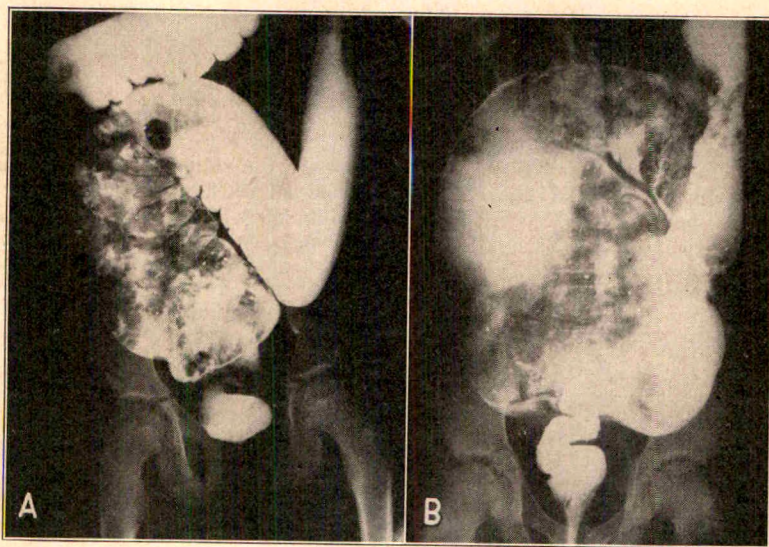


Fig. 12 (case 22).—A, roentgenogram showing the normal rectum and the normal lower portion of sigmoid flexure present below the enlarged and impacted upper sigmoid colon in an 11 year old boy. Evacuation of the colon was difficult. B, roentgenogram of the same patient showing enormous distention and impaction of the descending colon and the upper portion of the sigmoid colon. Medical management had been employed seven months. The normal rectum and lower sigmoid are again demonstrated.

only of large amounts of liquid petrolatum once or twice a week. Defecation occurred regularly. Episodes of distention and vomiting had not recurred. The abdomen was slightly protuberant and contained a soft impaction in the descending colon and the upper portions of the sigmoid flexure about 5 inches (12.5 cm.) in diameter. Eight quarts (7.5 liters) of barium sulfate suspension filled the greatly dilated sigmoid flexure and descending colon without passing on into the upper segments. The rectum and the lower portion of the sigmoid colon, examined digitally, proctoscopically and roentgenologically, were now moderately dilated. The patient assured us that it was time for him to take a heavy dose of liquid petrolatum and that this would effect adequate evacuation. This patient had undoubtedly been relieved of his earlier severe symptoms by the development of progressive dilatation of the

mass occupied the lower quadrants. The impacted stool could not be reached by rectal examination. The rectum was normal. Roentgen examination (fig. 12 A) revealed moderate dilatation of the entire colon, with extensive fecal impaction and enlargement of the descending colon and the upper portion of the sigmoid flexure. The rectum and the lower portion of the sigmoid flexure, as demonstrated by the use of an enema of barium sulfate, were normal. The colon was cleaned out during twelve days in the hospital by use of liquid petrolatum and enemas. Treatment with de-proteinized pancreatic extract was begun and continued for seven months. Spontaneous defecation occurred for the first time. Considerable improvement was noticed for five months. Two months later two episodes of impaction occurred and the patient was readmitted to the clinic. Roentgen examination showed

that the dilatation and impaction of the colon exceeded the original condition (fig. 12 B). The cecum contained hard fecal material. The colon was evacuated during three weeks in the hospital. Proctoscopic examinations toward the end of this period again revealed that the rectum and the lower portion of the sigmoid bowel, up to 12 inches (30.5 cm.), were normal. Deproteinized pancreatic extract and enemas were advised. The patient failed to return for further study or treatment.

A letter of inquiry four years later revealed that deproteinized pancreatic extract, enemas and daily doses of laxatives had all failed. The parents, by trial and error, discovered that evacuation could best be achieved by giving 1½ to 2 ounces (45 to 60 Gm.) of magnesium sulfate once a week with one smaller additional dose if necessary. The boy, although now 6 feet (183 cm.) tall, weighs 145 pounds (65.8 Kg.). Abdominal distention is moderate. This history illustrates well the occurrence of megacolon with the lower portion of the sigmoid flexure and the rectum normal and indicates the difficulty of management of this condition. It is possible that some dilatation of the lower portion of the sigmoid flexure and the rectum has occurred or will occur.

CASE 23.—H. L., a white boy admitted to the clinic at the age of 12 years and 15 years old at the time of his report, had obstipation, abdominal distention and vomiting in the first few days of life. Abdominal distention remained constantly through childhood. Spontaneous defecation never occurred. Enemas and laxatives were constantly employed. Attacks of vomiting and distention occurred and were relieved by enemas. Respiratory embarrassment was evident during these attacks. The abdomen at the time the patient was admitted was greatly distended. Large loops of colon, exhibiting occasional peristaltic movements, were visible. Rectal examination revealed a relaxed sphincter and a dilated rectum containing some gas and small particles of hard fecal material. Roentgen examination revealed moderate fecal impaction and dilatation of the upper part of the colon. The descending colon and the upper portion of the sigmoid colon reached a diameter of 7 inches (18 cm.). During one month's hospitalization repeated high enemas, liquid petrolatum and, later, mecholyl bromide partially decompressed the abdomen. A diagnostic spinal anesthesia produced no evident change in peristaltic activity. The patient was discharged receiving mecholyl bromide and liquid petrolatum, with enemas as required. The family physician reports that at the age of 15 the boy is much improved but far from normal. Defecation occurs daily with the aid of liquid petrolatum and mecholyl bromide. Abdominal distention is moderate. Visible colonic peristalsis is present. The thoracic cage is high with flaired costal margins. The patient carries on normal school activities. He is, however, poorly nourished.

CASE 24.—D. S., a white girl who is 20 years old at the time of this report, was admitted to the hospital four times, the first when she was 13, and followed in the clinic during the remainder of a period of fourteen months. Her parents died of tuberculosis, and the relatives with whom she lived knew little of her early history. At the age of 10 she was treated for tracheobronchial tuberculosis in a sanatorium for eight months and discharged with the process arrested. Daily doses of liquid petrolatum were required in the hospital because of constipation. When she was 11, episodes of

alternating diarrhea and constipation occurred and a diagnosis of Hirschsprung's disease and fecal impaction was established. Three or four days passed between evacuations. Cathartics, liquid petrolatum and enemas were employed. Multiple arthritic pains developed when the child was 13 and brought her to the hospital. A diagnosis of chronic infectious polyarthritis was made. The abdomen was moderately enlarged with the lower quadrants and the pelvis filled by a large mass of impacted fecal material. Some dilatation of the entire colon was visible. Rectal examination revealed an enormous rectum filled by a hard fecal impaction. Abdominal roentgenograms demonstrated the enlargement of the entire colon with the descending, sigmoid and rectal portions enormously distended. The colon was slowly evacuated by the use of a series of enemas, large quantities of liquid petrolatum and deproteinized pancreatic extract. The residual size of the colon and rectum is demonstrated in a roentgenogram (fig. 13) taken one month after the patient was admitted, when evacuation was almost complete. Proctoscopic and digital examination at this time showed that the rectum and descending colon had a diameter of 6 inches (15 cm.)

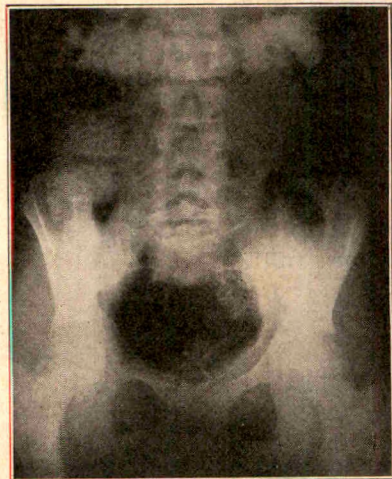


Fig. 13 (case 24).—Enormous residual size of the rectum of a 13 year old patient after evacuation of the megacolon by the use of repeated enemas, liquid petrolatum and deproteinized pancreatic extract. Recurring low fecal impaction gave symptoms of alternating constipation and diarrhea without abdominal distention or vomiting.

down to the sphincter muscle. The patient was treated for fourteen months, chiefly because of the arthritis. Rectal fecal impactions producing intermittent diarrhea and constipation recurred three times. Between impactions the abdomen remained flat and at times was scaphoid.

Follow-up correspondence reveals that at the time of this report the patient is living and well. She recently delivered a 7 pound (3,175 Gm.) baby. During pregnancy cascara sagrada was prescribed. Abdominal distention and fecal impaction have not recurred during the seven years that has elapsed since the last visit to the clinic. Defecation has been facilitated by taking 2 or 3 tablespoons (30 to 45 cc.) of liquid petrolatum once or twice a week. Enemas have not been employed. This history well illustrates the subsidence of symptoms of alternating diarrhea and constipation and obstruction

from fecal impaction associated with a megacolon that was most dilated in the lower part of the sigmoid colon and the rectum.

SUMMARY

Of 24 patients with megacolon (Hirschsprung's disease), 21 were treated by conventional medical management, consisting chiefly of diet, laxatives, enemas and parasympathomimetics, occasionally supplemented by sympathectomy. Three of the 21 patients required emergency laparotomy. A severe fecal impaction was removed through an incision in the colon in 1. Volvulus of the sigmoid colon was reduced in 2. One of these later underwent a partial resection of the sigmoid colon. Six of the 21 patients have undergone a remission of symptoms without surgical intervention and at an average age of 12 years are having regular daily intestinal evacuations. One patient underwent a remission of symptoms after sympathectomy and is well at the age of 17. Seven have continued to have mild to severe symptoms and at an average age of 15 are receiving medical treatment. Five patients, including 1 of the 3 who had a laparotomy, have died, 2 at the age of 15 months and 3 at the ages of 9, 17 and 24 years.

The remaining 3 of the 24 patients presented alarming symptoms and were treated by one stage resection of the megacolon and ileosigmoidostomy. These 3 are now living and well.

Medical management was supplemented by sympathectomy for 4 of the 24 patients. The gross pathologic picture was not significantly altered. One sympathectomized patient with a megacolon that terminated in an enlarged rectum improved and is living and well at the age of 17. Another with a megacolon also terminating in an enlarged rectum was clinically improved for three years and then died at the age of 24 with an acute impaction and perforation of the colon. Two others with an enlarged megacolon terminating in a normal lower segment of the sigmoid colon and a normal rectum experienced difficulty after sympathectomy. One died two months after operation, at the age of 15 months, of terminal pneumonia precipitated by abdominal distention during an attack of pertussis. In the other acute abdominal distention developed at the age of 11 and led to resection of the megacolon.

The patients reported in this study include all of those with megacolon examined since the opening of Duke clinic in 1930. It seems probable that at the present time they are younger than the patients normally encountered and that as time passes more of them will encounter difficulty.

The evidence derived from the clinical study seems to indicate that the megacolon involves the entire colon and rectum in 12 patients. It definitely involved the proximal segments of the colon and terminated in a segment of normal colon, usually low in the sigmoid flexure, and a normal rectum in 7 patients. In 5 of the patients the normal segment of sigmoid colon and the rectum dilated at times to permit difficult delivery of large fecal impactions to the anus and then, after the evacuation, resumed their normal size. Four of the 7 patients died. Three treated by resection of the megacolon are living. The megacolon definitely involved enormous segments of only the sigmoid and descending colon in 12 patients.

CONCLUSIONS

Significant conclusions are evident when the 24 case histories are grouped in accordance with the observed pathologicoanatomic changes rather than summarized in the conventional manner as a unit.

Group 1.—Uniform involvement of the entire colon terminating in a dilated or easily dilatable rectum occurred in 12 patients. Eight are now living, and evacuating their colons readily, at an average age of 10 years. One died three years after a sympathectomy, at the age of 24. Of the remaining 3, 1 is having moderately severe trouble at the age of 6, 1 required surgical reduction of a volvulus of the sigmoid colon at the age of 20 and 1 had a reduction of a sigmoid volvulus at the age of 59, with a recurrence three months later and resection of the sigmoid colon. It appears that protracted medical management of patients in this group is indicated as long as adequate nutrition can be maintained and persistent abdominal distention avoided. Sympathectomy does not alter significantly the gross pathologic conditions, and by interrupting visceral sensory pathways it may permit negligence on the part of the patient and the development of serious impactions. Segmental resection of the colon, as reported in the literature, has been followed frequently by recurrence of impactions proximal to the anastomosis. It would therefore seem that resection of the colon, if indicated for a patient with this condition, should start at the cecum and continue distally through the proximal divisions of the colon to the sigmoid region if necessary in order that the liquid contents of the ileum may empty into the remaining, and preferably rather short, segment of involved bowel.

Group 2.—Uniform dilatation of the proximal segments of colon terminating in a normal segment of bowel, usually in the sigmoid region

and a normal rectum occurred in 7 patients. Four receiving conventional management died, 2 at the age of 15 months, 1 at 9 years and 1 at 17 years. One had a sympathectomy. The remaining 3, with equally severe symptoms and with enormous megacolons, were treated at the ages of 2, 11 and 21 by resection of the megacolon and anastomosis between the terminal portion of the ileum and the remaining stump of normal sigmoid colon. One of them had previously had a sympathectomy. These 3 are living and well. Patients in this group demonstrated greater or more persistent abdominal enlargement than was observed in the other patients. It seems that when medical management fails to control obstipation and distention in patients with megacolon of this type and symptoms become alarming, colostomy or, if possible, resection of the megacolon is indicated.

Group 3.—Enormous enlargement of the sigmoid colon or of the sigmoid and descending colon, with or without involvement of the proximal portions of the colon and of the rectum, occurred in 5 patients. The 5 are now living, at an average age of 16, 2 free from symptoms and 3 with moderately severe symptoms. Three of these patients had definitely enlarged rectums, 1 had a normal rectum and in 1, during the course of observation, the rectum underwent a transition from normal to enlarged with relief of symptoms. Three of the patients inde-

pendently, by trial and error, have determined that laxatives taken once or twice a week produce more effective elimination than laxatives taken daily. It seems that protracted medical management of patients in this group is justified and that in patients with normal segments of lower sigmoid colon and normal rectums the structures may become progressively dilated and accomplish massive evacuations of impactions.

Careful examination of the distal portion of the colon of patients with Hirschsprung's disease by repeated rectal and proctoscopic examinations, and roentgen examination after enemas of barium and air; and of the proximal segments of the colon by roentgenography after oral administration of barium sulfate will aid in an understanding of the pathologic anatomy present and in a grouping of patients that may facilitate the prognosis and the choice between protracted medical management and resection of the colon. The examinations must be repeated after decompression of the colon, because normal rectums and normal segments of sigmoid colon may appear enlarged during the delivery of an impaction.

Dr. W. C. Davison, Dr. D. Hart, Dr. A. M. McBryde, Dr. J. Arena, Dr. A. H. London and Dr. J. A. Speed cooperated in the presentation of the clinical material.

Duke University School of Medicine.

MENINGOCOCCIC MENINGITIS

REVIEW OF ONE HUNDRED CASES

KURT GLASER, M.D.

CHICAGO

The cases of 100 consecutive patients with epidemic meningitis admitted at the Louisville General Hospital during the epidemic of 1943 are analyzed and discussed in this paper in order to throw some light on the problem of reduction of the death rate in future epidemics.

All patients with clinical signs and symptoms of meningitis were admitted to the isolation department of the hospital and a lumbar puncture was done immediately to confirm the diagnosis.

Of the 100 patients, 55 were men or boys and 45 were women or girls; 64 were white persons and 36 were Negroes. If one considers that the white population of Louisville is about six times as large as the Negro population, one can readily see that the number of Negro patients is relatively higher. This fact throws a significant light on the public health aspect of the problem and on the epidemiology of the disease. The difference in number can most likely be attributed to the poor and unhygienic housing and living conditions of the Negro portion of the population. The shift of large parts of the population due to war industries has also been contributory.

Of the 100 patients studied, 66 were in the first two decades of life and only 34 in the five following decades. Children under 5 years of age seem to be most susceptible. Of the 66 patients under 20 years of age, only 2 died, as compared with 15 of the 34 over 20.

SYMPTOMS

If it had been possible to obtain exact histories of all patients, they would have shown that "minor complaints" were even more common and of longer duration than our figures show. However, the mental state of 64 of the 100 patients at the time they were admitted to the hospital made it necessary to obtain the information from sources that were not always reliable.

Forty-four patients reported that they had "colds" prior to the development of the first meningeal symptoms. The question arises whether infection of the upper respiratory tract is a prodromal syndrome or an independent

disease that prepares the passages for invasion by the meningococci already lodged in the mucosa. Forty-seven patients reported that they had headaches for two or more days before they were hospitalized, and 6 had had this symptom for one or more weeks without investigating the possible cause. Twenty-seven patients had pains in the neck and back for two days or more before seeking medical aid. Forty-one patients vomited for two days or more and 11 for four days or more without investigating the cause.

The last symptom but by far the most characteristic is stiffness of the neck and back and opisthotonos. These symptoms usually lead the patient to the physician, although I recall 1 patient who walked into the emergency room with his head drawn back to such an extent that he had difficulty in keeping his balance.

These data show the order of appearance of the symptoms and also indicate that if the related facts could be brought to the attention of the public, patients would seek medical aid earlier in the course of the disease, a factor which is most important in the outcome, as shown in later tables. The education of the public in this matter constitutes another public health problem.

TREATMENT

It is felt that any delay in treatment reduces the chances for recovery. To obtain the fastest service and the greatest efficiency in spite of overcrowded departments and considerably reduced attending staff, a certain routine for handling most of the cases was established at the Louisville General Hospital during the epidemic of 1943. Each patient was transported without delay of admitting procedures to the examining room of the isolation department, and a lumbar puncture was performed immediately after the history was obtained and the physical examination performed. The leukocyte count and globulin content of the spinal fluid were obtained and a specimen treated with the Gram stain was examined within the first fifteen to thirty minutes. If the laboratory data confirmed the tentative diagnosis of meningococcic meningitis, the patient then received his first intravenous dose of sulfapyridine or sulfadiazine and a

From the Louisville General Hospital, Louisville, Ky.

cutaneous test for sensitivity to horse serum was done if it was thought to be necessary to administer antitoxin.

The average amount of sulfapyridine or sulfadiazine administered in twenty-four hours was $1\frac{1}{2}$ to 3 grains per pound (0.18 to 0.38 Gm. per kilogram) of body weight, divided into four to eight equal doses. The usual dose for an adult was 30 grains (1.8 Gm.), given every four hours. For children the first dose, given intravenously, consisted of about one half of the calculated daily dose, and for adults it was 5 Gm. After the first dose the drug was given orally or if necessary by nasal stomach tube. Administration was continued at the level indicated for three to five days and then at a reduced level for five to seven days before it was discontinued completely.

Meningococcus antitoxin was given in 40 cases. The decision as to the use of antitoxin was based on the clinical appearance of the patient. Thus 14 of the 17 patients who died and only 26 of the 83 who recovered were given antitoxin. I have felt that although the use of the sulfonamide drugs has reduced the death rate below that recorded in any previous reports, antitoxin might help some of the desperately ill patients who would not respond satisfactorily to treatment with the sulfonamide compounds. Since delay was to be avoided, all gravely ill patients received antitoxin when they were admitted to the hospital.

Two other factors may influence the outcome of the treatment. The first is the fluid balance. The patients received fluids by mouth, by stomach tube or by intravenous route according to their condition. The second factor is the sedation of the patient. My patients were not given any more sedatives than absolutely necessary; I preferred to restrain rather than to sedate them. I believe that this factor might be instrumental in the avoidance of localized lesions. A restless patient gives the purulent fluid less chance to induce adhesion. In no case in the series reported were repeated therapeutic lumbar punctures or intrathecal administration of antitoxin used.

RESULTS

Seventeen of the 100 patients died, 4 within twenty-four hours, 6 within thirty-six hours and 10 within forty-eight hours after they were admitted to the hospital. The mortality was equal in the groups treated with sulfapyridine and with sulfadiazine (table 1). Six of 8 patients who recovered from the acute stage but had sequelae were treated with sulfapyridine and only 2 with sulfadiazine. Whereas no fatal

toxic effects resulted from the administration of sulfapyridine, 1 of the 53 patients treated with sulfadiazine died with symptoms of urinary retention. (Unfortunately autopsy was not performed.) However, it should be added that in some cases the administration of sulfapyridine had to be discontinued and sulfadiazine used because of early toxic effects of the first drug.

TABLE 1.—*Results of Treatment with Sulfapyridine, Sulfadiazine and Antitoxin*

Treatment	Number of Patients	Number of Deaths	
		Total	After First 24 Hours of Hospitalization
Sulfapyridine			
Alone.....	28	6	0
Plus antitoxin.....	19	6	6
Total.....	47	6	6
Sulfadiazine			
Alone.....	32	5	2
Plus antitoxin.....	21	8	5
Total.....	53	11	7
Antitoxin plus one of the sulfonamide drugs.....	40	14	11

Study of such a small series permits only tentative conclusions as to the value of antitoxin in the treatment of meningococcic meningitis. Of the 17 patients who died, 14 were treated with antitoxin in addition to sulfapyridine or sulfadiazine (table 1). However, only the sickest patients were selected to receive antitoxin. Five of the 8 patients who showed complications had received 30,000 to 50,000 units of antitoxin. The presence of complications was probably related to the severity of the disease rather than to the administration of antitoxin (table 2).

TABLE 2.—*Data for the Eight Patients with Complications*

Complication	Treatment	
	Antitoxin Units	Sulfonamide Compound
Iritis.....	None	Sulfapyridine
Blindness; facial paralysis.....	50,000	Sulfapyridine
Iridocyclitis; deafness.....	50,000	Sulfapyridine
Deafness.....	30,000	Sulfapyridine
Blindness.....	None	Sulfapyridine
Blindness; deafness.....	30,000	Sulfapyridine
Blindness.....	None	Sulfadiazine
Arthritis.....	50,000	Sulfadiazine

The data presented in the section on symptoms indicate that the main reason for the failure of treatment is "delay." Nine of the 17 patients who died showed characteristic meningeal symptoms two or more days before they were admitted to the hospital. Indirect evidence of the detrimental effect of delay in the initiation of medical care is provided by the high percentage of deaths in the group of patients trans-

ferred from other hospitals, in other words, patients who had first been placed in other hospitals under different diagnoses (table 3). The mental state of many patients at the time of admission to the hospital also indicated that the disease had been present for some time. Of the 83 patients who recovered 35 (42.2 per cent) were rational and 48 (57.8 per cent) were not rational at the time of admission to the hospital. Of the patients who died only 1 (5.9 per cent) was rational and 16 (99.1 per cent) were not rational at that time.

TABLE 3.—Data for Patients Transferred from Other Hospitals

	Total	Patients Transferred	
		Number	Per Cent
Recovered.....	83	11	13.2
Died.....	17	6	35.3
Total.....	100	17	17.0

A program similar to that employed in the fight against infantile paralysis but applied locally in areas of epidemics should be of value in the reduction of the death rate from meningococcic meningitis. The public should be informed about early symptoms by posters, newspapers

TABLE 4.—Mental State of the Patients on Admission

	Number of Patients
Irrational.....	29
Semicomatose.....	16
Unconscious.....	5
Comatose.....	7
Lethargic.....	1
In convulsions.....	2
Drowsy.....	2
Stuporous.....	2
Rational.....	36

and radio addresses. The educational program should start at the onset of an epidemic and continue until the number of cases reported daily declines. Information should be extended through medical societies and medical journals to physicians in specialized practice as to the frequency of occurrence and the first symptoms and signs of the condition in each epidemic.

COMMENT

It can readily be seen that earlier medical attendance and proper diagnosis would reduce the death rate considerably. Though only 2 of the 100 patients had fulminating meningococcemia (Waterhouse-Friderichsen syndrome), which usually causes death within twenty-four

to forty-eight hours, 10 died within less than forty-eight hours after admission to the hospital. If these 10 patients are omitted from the series the death rate is reduced to 7 out of 90.

The high mortality among aged patients with meningococcic meningitis, the high incidence of the disease in crowded areas and the common occurrence of "colds" one or two weeks prior to the onset of the typical meningeal symptoms make the idea of preventive measures for exposed persons or if possible for the whole population in areas of poor living conditions at the onset of an epidemic appear advisable. The making of routine cultures of material from the nose and throat for all persons exposed has been tried, and it seems to be effective in the determination of carriers. The next steps would then be treatment of the carriers and prophylaxis for the persons exposed. This plan has been tried successfully in Army camps as reported recently by Kuhns, Nelson, Feldman and Kuhn¹ and others.

SUMMARY

An analysis of 100 cases of meningococcic meningitis indicated that delay in treatment due to failure to report to the physician at the occurrence of the first symptoms and to misdiagnosis was mainly responsible for the fatalities.

The incidence of the disease was greatest in crowded areas with unhygienic living conditions. The greatest number of patients were in the first two decades of life, but this group had the smallest number of deaths.

Sulfapyridine and sulfadiazine were found to be about equally effective against meningococcic meningitis with fewer complications from the use of sulfadiazine. Antitoxin did not seem to be of particular value.

Education of the public, information of physicians as to the peculiarities and progress of epidemics and improvement of living conditions seem to afford ways of attacking the problem. The prophylactic use of sulfonamide compounds as successfully tried in army camps would certainly be feasible in civilian institutions, but there would probably be great difficulty in applying it to large parts of the population.

707 Fullerton Avenue.

1. Kuhns, D. M.; Nelson, C. T.; Feldman, H. A., and Kuhn, L. R.: The Prophylactic Value of Sulfadiazine, J. A. M. A. 123:335 (Oct. 9) 1943.

Case Reports

TYPHOID

SUCCESSIVE INTESTINAL PERFORATIONS WITH RECOVERY

EDWIN PAUL SCOTT, M.D. AND ALVIN B. ORTNER, M.D.
LOUISVILLE, KY.

W. H., an 11 year old white boy, was admitted to the Children's Free Hospital Oct. 1, 1942. The clinical history was obtained from the child's father. The chief complaint at the time of admission was the presence of fever for the past ten days.

History.—Four weeks prior to admission the patient began having headache, fever and anorexia. He was seen by the family physician at the onset of the illness. Treatment was symptomatic, consisting of administration of cathartics, antipyretics and rest in bed. Under this regimen there was a remission of symptoms. The child had no complaints and was allowed to be ambulatory. The remission lasted for one week. On Sept. 13, 1942 he again had headache and anorexia. Two days later there was a recurrence of the fever accompanied by general malaise, and the boy was again confined to bed. The fever continued, and vomiting occurred. Four days later thin yellow diarrheal stools were noted. Ten days before the boy was admitted to the hospital the fever became higher and the vomiting increased. The patient became delirious three days before being brought to the hospital. Delirium, fever, vomiting and anorexia continued until after the patient entered the hospital. On Oct. 1, 1942, nine hours prior to admission, the child experienced a sudden sharp pain in the right lower quadrant of the abdomen which lasted for approximately thirty minutes.

On inquiry it was learned that other people living in the vicinity and using the same water supply were reported to have typhoid. The patient had never been immunized against typhoid.

Physical Examination.—When the patient was admitted to the hospital, he was semiconscious and appeared to be both acutely and chronically ill. There was severe emaciation and dehydration. On the left cheek there was a port wine stain of a small hemangioma. The lips and pharynx were dry. Scattered over the skin there were numerous white papulovesicular lesions but no rose spots. The chest was normal. The abdomen was scaphoid, and respiratory motion of the anterior wall of the abdomen was limited. On palpation there were noticeable spasm and tenderness throughout, with rebound tenderness at the site of pressure. Just below the left costal margin the edge of the spleen could be palpated. On auscultation an occasional peristaltic wave could be heard. Rectal examination revealed bilateral tenderness anteriorly. The temperature was 99.4 F., and the pulse rate was 120 and the respiratory rate 38 per minute.

Laboratory Data.—The red cell count was 4,090,000 per cubic millimeter, with 13 Gm. of hemoglobin per hundred cubic centimeters of blood. The white cell count was 10,800 per cubic millimeter. The differential smear revealed 65 per cent polymorphonuclear leukocytes, 17 per cent lymphocytes, 2 per cent eosinophils, 3 per cent myelocytes and 13 per cent "stab" cells. Urinalysis revealed albumin (2 plus).

From the Department of Pediatrics, the services of Dr. James W. Bruce and Dr. W. W. Nicholson, and the Department of Surgery, University of Louisville School of Medicine.

A roentgenogram of the abdomen taken with the patient in the upright position revealed dilatation of the large and the small bowel but no free subdiaphragmatic air or fluid.

Diagnosis.—The provisional diagnosis was typhoid complicated by intestinal perforation.

Preoperative Clinical Course.—Surgical consultation was obtained shortly after the patient was admitted, and it was agreed that early exploration should be done. Because of the extremely poor condition of the patient, the preoperative period was lengthened so that the fluid and electrolyte balance could be restored by parenteral administration of fluids.

Five per cent dextrose in isotonic solution of sodium chloride was given by the continuous intravenous drop method, and 300 cc. of citrated whole blood was administered.

Intestinal drainage was instituted by use of a Levine tube and a Wangenstein apparatus.

On October 2, fifteen hours after the patient was admitted, an operation was performed (A. B. O.).

Operation.—With the patient under drop ether anesthesia, the peritoneal cavity was entered through a right pararectus incision extending from 2.5 cm. above to 7.5 cm. below the umbilicus. When the peritoneal cavity was opened a mild fecal odor was noted. There was a small amount of free, turbid peritoneal fluid. The serosa covering the loops of the small intestine was hyperemic and partially covered with fibrin. Examination of the ileum revealed that the Peyer patches were greatly thickened, edematous and extremely hyperemic, the condition being most evident in the distal third. Approximately 30 cm. from the ileocecal junction there was a perforation of the ileum 0.5 cm. in diameter, sealed with omentum. Another perforation, 0.3 cm. in diameter, was found in the ileum, 2 cm. from the ileocecal junction. Both perforations were closed transversely to the long axis of the intestine by two tiers of Lembert sutures of fine silk, and a small quantity of sulfanilamide crystals was dusted between the tiers. One other Peyer patch had a light green exudate over it and appeared ready to "blow out." This area was reinforced by a single tier of Lembert sutures. Four grams of sulfanilamide crystals was then dusted into the peritoneal cavity and the edges of the wound. The wound was closed in layers with interrupted silk sutures. No drainage was instituted.

A culture of peritoneal fluid taken at the time of operation revealed typhoid bacilli.

Postoperative Course.—The patient was placed in Fowler's position in an oxygen tent. The Levine tube which had been placed in the stomach prior to the operation was again connected to a Wangenstein apparatus. Intravenous administration of 5 per cent dextrose in isotonic solution of sodium chloride was continued. This was followed by a transfusion of citrated whole blood.

On the first postoperative day Wangenstein suction was discontinued. The patient was put on a high caloric, high vitamin, liquid diet and was given succinylsulfathiazole. The initial dose was 2.5 Gm., with subsequent doses of 1.25 Gm. every four hours. Food was given

realed normal motion of both sides of the diaphragm. The reaction to the cephalin-cholesterol flocculation test was elevated to 3 plus, but the bilirubin content of the blood was within normal limits. The stool cultures remained negative, but on December 7, for the first time, the urine contained typhoid bacilli. In view of this it was considered that the fever was caused by a recrudescence of typhoid.

Supportive treatment was continued. The general condition of the patient improved, but he continued to have a low grade fever.

On December 26 he suddenly had an acute colicky abdominal pain. Examination revealed generalized abdominal tenderness, with noticeable distention. Rectal examination revealed no symptoms. A diagnosis of intestinal obstruction due to adhesions was made, and the peritoneal cavity was again explored (A. B. O.). The exploration was carried out with the patient under ether anesthesia, and the abdomen was entered through the old wound. The jejunum and the upper part of the ileum were distended, and the obstruction was found to be due to many dense adhesive bands in the region of the previous ileostomy. The appendix, which was bound down in the adhesions, was resected to facilitate the lysis of adhesions. During the dissection the ileum at the side of the previous ileostomy was inadvertently opened, and another ileostomy was therefore performed. The pathologist's report on the appendix described chronic infectious granuloma resembling that of typhoid.

The postoperative course was uneventful. The temperature became normal on the fourth day after the

operation. On Jan. 5, 1943 the ileostomy tube was removed, and drainage ceased shortly thereafter. On January 21, the one hundred and thirteenth day of hospitalization, the patient was discharged.

Subsequent visits to the clinic revealed a satisfactory convalescence.

On April 25 the patient was again admitted to the Louisville General Hospital with a history and physical symptoms suggestive of intestinal obstruction. Treatment was conservative, and within forty-eight hours he was asymptomatic. He was discharged April 28.

On November 6, thirteen months after the original admission, the boy was in an excellent state of nutrition, and he was attending school. His only complaint was an incisional hernia, for which he was wearing an abdominal support.

SUMMARY

An 11 year old boy with typhoid survived successive multiple intestinal perforations. In a review of the literature we have been unable to find a report of survival of typhoid complicated by successive multiple intestinal perforations.

We believe that early surgical intervention is indicated for intestinal perforation due to typhoid and that it was largely responsible for the recovery of this patient.

University of Louisville School of Medicine.

FATAL STATUS EPILEPTICUS

M. G. PETERMAN, M.D.

MILWAUKEE

AND

KURT GLASER, M.D.*

CHICAGO

Status epilepticus is a rare but serious complication of idiopathic epilepsy in children. In adults it is often fatal. However, in twenty-two years of special interest in epilepsy one of us, M. G. P., had not seen a patient in whom the condition was fatal or resisted all treatment. A recent case is presented because status epilepticus developed after the child had been on a fasting diet for four days and because she did not respond to treatment that exhausted our resources.

REPORT OF A CASE

R. P., a white girl, was first seen by one of us (M.G.P.) Nov. 6, 1935, at 5 years of age. She had had convulsions for one year. Physical examination revealed only fatigue posture and dental caries. On the basis of the history and a description of the seizures a diagnosis of idiopathic epilepsy was made. The child was given a high fat (not weighed), low fluid (1,000 cc. daily) diet with 0.032 Gm. of phenobarbital three times a day. Administration of phenobarbital was discontinued by the parents after about six months. The patient was well and free of seizures until Oct. 1, 1942. Seizures then recurred and were described as dizzy spells with tonic and clonic spasms but with no loss of consciousness and no loss of control of the sphincters. The seizures were preceded by auras of gastric uneasiness. The family physician prescribed phenobarbital again, but the seizures increased in severity and were accompanied with loss of consciousness as they decreased in frequency.

The patient's birth was essentially normal. She was a full term infant with a normal delivery. She had had measles and mumps. Her progress in school was normal. One of the mother's sisters had lost 2 children with convulsions in infancy.

The patient was admitted to the Milwaukee Children's Hospital on Oct. 5, 1943, at the age of 12 years, for treatment in the private service of one of us (M. G. P.). Physical examination revealed a well developed, well nourished child with normal mentality. The left ankle was swollen, painful and tender, with an area of ecchymosis on the lateral aspect (the child was said to have injured her ankle in a recent fall). The neurologic examination revealed no abnormality, and the optic disks appeared to be normal. The blood count and the urine were normal. The blood contained 80 mg. of sugar, 10.4 mg. of calcium and 5.1 mg. of phosphorus per hundred cubic centimeters. The electroencephalogram made in the office of one of us (M. G. P.) Oct. 5, 1943, showed recurring delta activity, with seven per second waves.

*Formerly chief resident, Milwaukee Children's Hospital.

The patient was given a fasting diet which consisted of 1,000 cc. of unsweetened orange juice and 1,000 cc. of clear diabetic broth with six cellulose wafers (no food value) a day. On October 7 she had three mild grand mal convulsions. On October 8 she had two convulsions and her temperature rose to 102.6 F. (rectal). On October 9 there were four convulsions, but the temperature receded to 100.4 F. (rectal). On October 10, beginning at 10 p. m., the patient had four seizures in forty-five minutes. The last seizure was longer and more severe than any of the previous ones and was followed by deep, exaggerated respiration. The patient received 0.032 Gm. of phenobarbital at two to four hour intervals. The urine contained acetone (2 plus reaction) and a faint trace of diacetic acid. The seizures became more frequent; there were nine convulsions between 7 and 8 p. m. The danger of impending status epilepticus was considered. The dose of phenobarbital was increased; 0.032 Gm. of diphenylhydantoin sodium was given, and sweetened orange juice was administered to counteract possible hypoglycemia. In the early morning of October 11 the convulsions continued at eight minute intervals and vinyl ether was given. The patient relaxed completely. Two cubic centimeters of 50 per cent solution of magnesium sulfate was injected intramuscularly. At 8 a. m. a spinal tap was done to relieve the intracranial pressure. After the first 4 cc. of fluid was removed, the patient went into another seizure, maintaining the exact eight minute interval between seizures. The needle was removed and reinserted after the convulsion. Another 10 cc. of fluid was removed. The patient returned to bed awake and in good condition, complaining of headache. Two or three minutes later, after the usual interval, another convulsion occurred. Later during the day 0.1 Gm. of diphenylhydantoin sodium was given, and 10 cc. of 10 per cent solution of calcium gluconate was injected intravenously. The patient was anesthetized with ether, which had only a short effect. The convulsions continued, and chloroform was administered by the anesthetist. One-tenth gram of sodium amylal was then given intramuscularly. At 5 a. m. October 12 0.23 Gm. of sodium amylal was given intravenously. The convulsions continued at short intervals. Ether kept the patient asleep for about thirty minutes but did not stop the convulsions. One hundred and seventy convulsive seizures occurred in twenty-four hours. The temperature had risen to 106.4 F. (rectal), and tepid sponges, ice packs and cooling enemas were used. Two hundred cubic centimeters of 10 per cent solution of dextrose in isotonic solution of sodium chloride was given intravenously. Codeine, 0.065 Gm., was given subcutaneously and 0.1 Gm. of phenobarbital orally. Two grams of chloral hydrate was administered in a starch enema. Chloroform was administered again by the anesthetist. Three ampules (0.375 Gm.) of sodium amylal were given intravenously. The patient

was almost exhausted. The convulsions were four or five minutes apart; the temperature ranged between 99 and 106 F. (rectal), and the blood pressure was 128 mm. systolic and 72 diastolic. On October 13, 0.00065 Gm. of scopolamine hydrobromide was given every four hours, and solution of tribromoethanol U. S. P. was given by rectum after another attempt to produce anesthesia with chloroform and with ether. The convulsions continued. Twenty-four cubic centimeters of paraldehyde and 24 cc. of liquid petrolatum were given rectally. The patient gradually went into a state of exhaustion. The convulsions decreased and became less severe. The pupils were fixed; the pulse rate went up to 160, and the pressure decreased. At times there was Cheyne-Stokes respiration. On the morning of October 14 the pulse became still weaker; the respirations were 40 per minute and deep. The hands and feet became cold and the skin mottled. The patient appeared to be dying. The convulsions ceased completely, and the patient died at 10:46 a. m., October 14. The terminal temperature was 107.4 F. (rectal).

A necropsy was performed two and one-half hours post mortem by Dr. G. H. Hansmann. He reported that the conditions were essentially normal except for the following: "The right side of the heart was greatly dilated, and the microscopic section revealed edema. The liver weighed 1,750 Gm., and the cut section was pale and appeared to contain no cloudy swelling. Microscopically, fatty degeneration of the periphery of the lobules was found, and all other cells of the liver revealed fatty degeneration of lesser extent. The spleen was congested. The brain weighed 1,320 Gm., and the veins stood out as somewhat dilated and engorged vessels containing unusually dark blood. The brain was symmetric, which would indicate that there was no internal lesion. The meninges were searched for scars, for evidence of a point of initiation of the spasms; but none was found. Microscopic examination of the brain revealed areas of acute edema. The

nerve cells were triangular and elongated. The nerve processes could be traced for a considerable distance, and there was no evidence of an inflammatory reaction. Examination of other sections of the brain revealed petechial hemorrhages and small cavities throughout the white matter, particularly in the region of the internal capsule. The cavities measured up to 2 mm. in diameter. There were no other gross abnormalities. Microscopic examination of the sections revealed small cysts and congestion of some of the vessels. Other vessels were collapsed, and the Virchow-Robin spaces were large and filled with blood. This condition was particularly prominent in the region of the internal capsule and midbrain and was taken to indicate cerebral anoxia."

SUMMARY

A 12 year old girl in excellent physical condition except for idiopathic epilepsy died of exhaustion after ketosis had developed. The ketosis was counteracted with no effect. The following drugs, listed in order of their administration, produced no effect on the convulsions: phenobarbital (orally and subcutaneously), diphenylhydantoin sodium (orally), magnesium sulfate (orally, intramuscularly and rectally), calcium gluconate (intravenously), vinyl ether (inhalation), sodium amytal (intramuscularly and intravenously), chloral hydrate (rectally), ether (inhalation), codeine (subcutaneously), chloroform (inhalation), tribromoethanol (rectally), scopolamine hydrobromide (subcutaneously) and paraldehyde (rectally).

Milwaukee Children's Hospital, Milwaukee.
Children's Memorial Hospital, Chicago.

Progress in Pediatrics

POLIOMYELITIS

III. ANALYSIS OF RESULTS FOLLOWING TREATMENT AS REPORTED IN THE RECENT LITERATURE

JOHN A. TOOMEY, M.D., AND PAUL M. KOHN, M.D.

CLEVELAND

In a previous communication¹ we analyzed the results obtained in a series of patients with poliomyelitis treated according to the Toomey-Feiss method. The reader is referred to that article for the classification of types, statuses and substatures or conditions. In the present review we shall try to analyze, in comparable fashion, the results obtained in other clinics in which different methods of treatment were employed. Some reports do not include adequate facts, and comparison is therefore impossible. In such instances only our impression can be given.

KENNY TREATMENT

Cases Reported by Pohl.—The first series of cases in the United States in which the Kenny treatment was used was described by Pohl in 1942.² Since that time no other cases have been described in detail from the poliomyelitis clinic of the Minneapolis General Hospital, to our knowledge, although mention has been made of 28 more cases. The conditions in the spinal fluid were not mentioned in the report on the original series of 26 cases.

In an analysis of the results reported by Pohl, cases 2, 16 and 20, in which there was no paralysis, can be excluded, since the patients should have recovered with little or no treatment. In case 13 treatment might not have been needed. The 2 cases of bulbar poliomyelitis (cases 10 and 24) should also be excluded; it would be a rash person indeed who would claim that external treatment affected the bulbar nerves. We included case 8, although in our service a detailed neurologic examination would have been performed before the patient was accepted as having poliomyelitis, especially since his symptoms fit toxic neuronitis so well.

From the Department of Contagious Diseases, City Hospital and the Department of Pediatrics Western Reserve University.

1. Toomey, J. A., and Kohn, P. M.: Poliomyelitis: II. Results of Treatment During the Acute Stages of the Disease, *Am. J. Dis. Child.* **67**:393-399 (May) 1944.

2. Pohl, J. F.: Kenny Treatment of Anterior Poliomyelitis (Infantile Paralysis): Report of First Cases Treated in America, *J. A. M. A.* **118**:1428-1433 (April 25) 1942.

Of the 26 patients described by Pohl, 3 were in group 4 and 2 in group 5D alpha. These patients required no treatment in order to recover satisfactorily. Of the other 21 patients, for whom treatment might have influenced recovery, 5 (23.8 per cent) were completely cured. If the 2 patients in 5D alpha are included, 7 of 23 patients (30.4 per cent) were completely cured.

TABLE 1.—Classification of Pohl's Patients Treated by the Kenny Method

No.	Group	Status		No.	Group	Status	
		Before	After			Before	After
1	5 B	IV	III	14	5 B	III	III A
2	4	I	I	15	5 B	III	III C
3	5 B	IV	IV A	16	4	I	I
4	5 D beta	III	I	17	5 B	IV	IV B
5	5 C	IV	III	18	5 B	III	III B
6	5 B	IV	III	19	5 B	III	III A
7	5 B	IV	III	20	4	I	I
8	5 B	IV	I	21	5 B	III	III A
9	5 B	III	III C	22	5 B	II	I
10	5 D alpha	III	I	23	5 B	III	II
11	5 B	III	III B	24	5 D alpha	III	I
12	5 A	II	I	25	5 B	IV	IV B
13	5 E alpha	II	I	26	5 C	III	III C

Five of the 21 patients (23.8 per cent) advanced one or more statuses. Ten (47.6 per cent) of the 21 patients who required treatment were cured or advanced one or more statuses. Of the 11 patients who did not improve at least one status, 4 (36.3 per cent) improved to condition A, 4 (36.3 per cent) to condition B and 3 (27.4 per cent) to condition C. None failed to show improvement.

Analyzing the data by groups and statuses, we find the following distribution:

Classification Before Treatment		Number of Patients	Classification After Treatment, Status
Group	Status		
4	I	3	I
5 A	II	1	I
5 B	II	1	I
	III	1	II
		3	III A
		2	III B
		2	III C
	IV	1	I
		3	III
		1	IV A
		2	IV B
5 C	III	1	III C
	IV	1	III
5 D alpha	III	2	I
5 D beta	III	1	I
5 E alpha	II	1	I

If the 3 nonparalytic patients (group 4) and the 2 in group 5D alpha who improved to status I are added to the 5 who recovered completely, 10 of 26 (38.4 per cent) were completely cured.

The results are good. Statistical analyses do not reflect subjective well-being and degrees of passive mobility. One must agree with Pohl that to appreciate these the patients should be seen.

Cases Reported by Daly and His Associates.—Daly, Greenbaum, Reilly, Weiss and Stimson³ attempted to evaluate the Kenny method in the early treatment of poliomyelitis. Of 71 patients admitted to the Willard Parker Hospital in New York during the epidemic of 1941, 43 were treated by so-called orthodox methods and 28 by the Kenny method.

Results of Treatment by Orthodox Methods.—Forty-three patients with spinal poliomyelitis admitted to the Willard Parker Hospital between Aug. 8 and Sept. 23, 1941 were treated by so-called orthodox methods. A detailed analysis of the involvement of muscles was not reported, and loss of function rather than muscular involvement was stressed. Nevertheless, it was felt that the description was sufficiently clear to classify patients according to our schema.

Daly and her associates stated that at the present time only symptomatic treatment is indicated for early poliomyelitis, a sweeping conclusion which is not justified by our experience during the past twenty-two years. Statements to the effect that patients with bulbar paralysis respond well to treatment cannot be accepted at face value in view of the fact that there has been a gradual but steady increase in the number of patients with bulbar symptoms and a decrease in the mortality in this group in recent years. Improvement in bulbar paralysis has nothing whatever to do with treatment.

Fifteen patients had no follow-up examinations. Nine of them were in group 5B; 1 was in group 5C; 2 were in group 4, and 3 were in group 5D alpha. In addition, there were 5 patients in group 4, 1 in group 2 and 4 in group 5D alpha. In all there were 10 patients who did not require actual treatment for a satisfactory recovery. Thus 25 of the 43 cases could not be considered in an evaluation of any treatment.

Of 18 patients who required treatment and for whom follow-up examinations were performed, none were completely cured. Three of the 5

patients in group 4 and 1 patient in group 2 (66.6 per cent) had residual spasm or spinal curvature. One (5.5 per cent) of the 18 patients improved one status. However, this patient, who was in group 5B and improved from status IV to III, had a residual contracture. Seventeen of the 18 patients considered in the evaluation of treatment did not improve enough to reach another status; nevertheless, some improvement occurred. Three patients (17.6 per cent) improved to condition A, 3 (17.6 per cent) improved to condition B and 2 (11.8 per cent) improved to condition C. Nine patients (52.8 per cent) showed no improvement.

Analyzing the data by groups and statuses, we find the following distribution:

Classification Before Treatment		Number of Patients	Classification After Treatment, Status
Group	Status		
2	I	1	I (residual spasm)
4	I	5	I (residual spasm in 3)
5 D alpha	II	1	II B
	III	2	III A
		1	III B
5 D beta	III	1	III A (residual spasm)
		1	III C
5 B	III	2	III A
		2	III B
		1	III C
	IV	7	III
		1	III
		2	IV
5 C	V	1	V A

If the nonparalytic patients (groups 2 and 4) and the patients with bulbar poliomyelitis (group 5D alpha) are included, the total number considered is 28. Of these only 2 patients (7.1 per cent), who were in group 4, were discharged as completely cured.

TABLE 2.—Classification of Daly's Patients Treated by the Orthodox Method

No.	Group	Status		No.	Group	Status	
		Before	After			Before	After
1	5 D alpha	II	II B	23	5 B	III	NF
2	4	I	I	24	5 B	III	III B
3	5 D beta	III	III C	25	5 B	III	III
4	4	I	I	26	5 B	III	III
5	4	I	I(s)*	27	5 B	III	III
6	4	I	I(s)	28	5 B	III	III
7	4	I	I(s)	29	5 B	IV	IV
8	2	I	I(s)	30	5 B	III	III
9	4	I	NF†	31	5 B	III	NF
10	4	I	NF	32	5 C	V	V A
11	5 D alpha	III	NF	33	5 B	III	NF
12	5 D alpha	III	NF	34	5 B	IV	NF
13	5 D alpha	III	III A	35	5 B	III	III
14	5 D alpha	III	III B	36	5 C	IV	NF
15	5 D alpha	III	III A	37	5 B	IV	NF
16	5 D alpha	III	NF	38	5 B	IV	NF
17	5 D beta	III	III A (s)	39	5 B	IV	NF
18	5 B	III	III A	40	5 B	III	NF
19	5 B	III	III B	41	5 B	III	III
20	5 B	III	III C	42	5 B	III	NF
21	5 B	IV	III	43	5 B	IV	IV
22	5 B	III	III A				

* (s) indicates residual spasm or spinal curvature.

† NF indicates that the patient was not followed up.

3. Daly, M. M. I.; Greenbaum, J.; Reilly, E. T.; Weiss, A. M., and Stimson, P. M.: Early Treatment of Poliomyelitis with Evaluation of Sister Kenny Treatment, J. A. M. A. 118:1433-1443 (April 25) 1942.

Results of Treatment by the Kenny Method.—Of the 28 patients treated by the Kenny method, there were 2 in group 4 and 5 in group 5D alpha, 7 in all for whom treatment was unnecessary. This leaves 21 patients whose progress could be evaluated. Only 1 patient (4.7 per cent) was completely cured. Three others (14.3 per cent) advanced at least one status. If these are combined, there were 4 patients (19.0 per cent) who advanced one or more statuses. Of the 17 patients who did not advance one status, 4 (23.4 per cent) improved to condition A, 11 (64.9 per cent) improved to condition B and 2 (11.7 per cent) improved to condition C.

Analyzing the data by groups and statuses we find the following distribution:

Classification Before Treatment		Number of Patients	Classification After Treatment
Group	Status		Status
4	I	2	I
5D alpha	III	4	III B
		1	III C
5D beta	III	1	II
		2	III B
		1	III C
5A	III	1	II
5C	III	2	III B
	IV	1	IV B
5B	III	1	I
		1	II
		2	III A
		4	III B
		1	III C
	IV	2	IV A
		2	IV B

If the 2 patients with nonparalytic poliomyelitis (group 4) and the 5 with bulbar poliomyelitis (group 5D alpha) are included in the computations, there are 28 patients to be considered. Of these only 2 patients in group 4 and 1 in group 5B were discharged as cured (10.7 per cent).

TABLE 3.—Classification of Daly's Patients Treated by the Kenny Method

No.	Group	Status		No.	Group	Status	
		Before	After			Before	After
44	4	I	I	58	5B	III	III A
45	4	I	I	59	5A	III	II
46	5D alpha	III	III B	60	5B	III	III B
47	5D alpha	III	III B	61	5B	IV	IV B
48	5D alpha	III	III C	62	5B	III	III B
49	5D alpha	III	III B	63	5B	III	III B
50	5D alpha	III	III B	64	5B	III	III A
51	5D beta	III	III B	65	5B	III	I
52	5D beta	III	III B	66	5C	IV	IV B
53	5D beta	III	III C	67	5B	IV	IV A
54	5D beta	III	II	68	5B	IV	IV A
55	5C	III	III B(s)*	69	5C	III	III B
56	5B	III	II	70	5B	IV	IV B
57	5B	III	III C	71	5B	III	III B

* (s) indicates residual spasm or spinal curvature.

Cases Reported by Coon.—Coon⁴ reported that 8 patients ranging in age from 2 months to

4. Coon, H. M.: Wisconsin Experience with Kenny Treatment Methods, Wisconsin M. J. **42**:783-784 (Aug.) 1943.

17 years were treated according to the Kenny method with the assistance of Kenny-trained personnel at South View Hospital in Milwaukee. Three of the 8 (37 per cent) left the hospital completely cured. The other patients had no deformities, although they had slight muscular weakness and some residual paralysis. The results, in the opinion of Dr. Fox, medical director of the hospital, were most encouraging. At the Wisconsin General Hospital in Madison 21 patients were treated, 3 of whom died of bulbar poliomyelitis. Fourteen of the 21 (66 per cent) were discharged from the hospital with definite improvement.

We could not compare the results reported by Coon with those of other investigators, since no information was given about the exact condition of the patients before treatment was started. The types of disease were not defined and the exact amount of improvement present when the patients left the hospital was not indicated. There were no detailed reports of cases.

Cases Reported by Wilder.—Wilder⁵ treated 40 patients by the Kenny method; 10 (25 per cent) were discharged as normal within an average of 29.2 days, and 1 died. Eleven of the patients who remained in the hospital at the time of the report were up and walking, and the other 18 were progressing satisfactorily. Only 1 patient needed braces. Wilder stated that a large percentage of the patients previously treated by him by other methods needed braces, but he gave no descriptive evidence to substantiate the statement.

The report illustrates the fact that unless the types of patients treated are thoroughly described an analysis cannot determine how much credit should be given a treatment used. It is unfortunate that the statistics were not given in more detail, since they seemed to denote a trend.

Cases Reported by Dyson.—Dyson⁶ described the results of treatment of 39 patients by the Kenny method. He stated that most of the patients did not have severe poliomyelitis. Only 2 were bedridden, and many had no definite weakness, having had only spasm of the muscles of the neck and back and of the hamstring muscles. Such a condition is present with any meningeal irritation and disappears automatically in due time without treatment, although in our opinion recovery may be hastened by early

5. Wilder, M. J.; Kenny Treatment of Poliomyelitis, Kentucky M. J. **41**:45-47 (Feb.) 1945.

6. Dyson, J. E.; Kenny Treatment in Acute Poliomyelitis: Report of First Year at Iowa Lutheran Kenny Cottage, J. Iowa M. Soc. **33**:375-379 (Aug.) 1943.

physical therapy. One patient died. Analysis of the statistics was complicated by the fact that patients had roentgen therapy. In analyzing statistics relating to recovery from poliomyelitis, when it is noted that 28 patients, nearly 72 per cent of the series, became completely well one must bear in mind that most of the patients may have had only so-called muscular spasm and the related symptoms of meningeal irritation.

In Dyson's experience spasm was persistent despite treatment; 4 of the patients who became ill in 1940 were still spastic when the article was written, in 1943.

The author made a significant statement which should be borne in mind, that is, that "overactivity has brought back muscle spasms and changed functions of arms, backs and legs in some who thought they were well." No comment is necessary. One may ask whether muscular power and function should not have been tested and splinting done if necessary.

The length of time spent in the hospital did not parallel the duration of the attack.

It was impossible to analyze the cases according to our classification, since the percentage of muscular movement was not stated. Nevertheless, a rough attempt was made. If we designate the patients by number in the order in which they are listed in Dyson's master table, patients 1, 4, 6, 8, 9, 11 and 16 probably belonged in our groups 1 to 4 and patients 2, 3, 5, 10, 12, 13, 14, 17, 21, 23, 24, 25, 26, 27, 28, 35 and 36 probably belonged in our group 5A (patients with fleeting weakness in various groups of muscles, who recover with a minimum of physical therapy). Patients 7, 15, 18, 19, 20, 22, 29 and 30 and possibly 31, 32, 34, 37, 38 and 39 probably belonged in our group 5B; as nearly as we were able to determine, they were not completely well at the time the report was issued.

If 28, or 71 per cent, of 39 patients were completely well, as claimed by the author in the body of the paper, how can one account for the fact that those listed above as belonging in group 5B still had the conditions described in the table? Probably the author had in mind functional recovery. It is unfortunate that these statistics could not be analyzed, for there seems to have been distinct improvement after treatment.

Cases Reported by Bingham.—Bingham⁷ in a monograph reported the results for 48 patients treated by the Kenny method. He did not present the cases in detail, and the data cannot

be analyzed. We felt, however, that the evidence was sufficient to show that the patients had neither contractions nor deformities after the treatment. We cannot tell how quickly the patient progressed or the status of the residual weakness.

Bingham probably referred to the same 48 patients in a subsequent article.⁸ Although the patients seemed significantly better, the author stated that final conclusions on the merit of the new treatment should be determined from the amount of paralysis and deformity in the years to come. The author also recognizes the fact that some improvement, rather than being due to the Kenny treatment, might have been due to the fact that the patients had mild abortive poliomyelitis and would have recovered anyway. Bingham should have mentioned whether deformities and contractions developed during treatment, especially in patients for whom the Kenny therapy was employed, since a cardinal point has been made that no deformities or contractions develop in patients who receive this treatment.

Cases Reported by Stuck and Loiselle.—From the San Antonio epidemic of 1942, 87 cases were described by Stuck and Loiselle.⁹ Routine spinal punctures were not made in all instances, because, as the authors stated, the diagnosis was sufficiently clear to eliminate the necessity of such a procedure and in patients with stiff backs spinal puncture was too painful. It is dangerous to adopt such criteria. In all probability some of the patients with symptoms had the disease; but because so many other infections can be mistaken for abortive poliomyelitis and because the effect of a therapeutic procedure was to be determined, the authors should have proved their diagnoses beyond a doubt.

Stuck and Loiselle also stated that nearly all patients with bulbar poliomyelitis died despite the use of a respirator. These are the very conditions under which the use of a respirator is contraindicated unless the patient has concomitant paralysis of the intercostal muscles and the diaphragm. A respirator cannot be expected to benefit a patient with bulbar poliomyelitis; in fact, it aggravates his condition.

It is difficult to analyze the statements of Stuck and Loiselle. They did not describe the amount of paresis or paralysis the patients had before they were treated. They stated that 2 patients who were not treated showed contraction. This has been the experience of every one.

7. Bingham, R.: Kenny Treatment for Infantile Paralysis: Comparison of Results with Those of Older Methods of Treatment, *J. Bone & Joint Surg.* **25**:647-650. (July) 1943.

8. Bingham, R.: Unpublished monograph.

9. Stuck, W. G., and Loiselle, A. O.: The 1942 San Antonio Poliomyelitis Epidemic, *J. A. M. A.* **122**:853-855 (July 24) 1943.

It is not known whether the 2 patients with polyneuritic paralysis had painful neuritis only; but, taking for granted that this was so, the data for 33 patients in all, 25 with abortive poliomyelitis, 6 who died and 2 who had polyneuritis, would have to be excluded from consideration of the value of the therapy. If the 2 patients with polyneuritis are included, there were 56 patients who needed treatment. The data presented show that at the end of a course of treatment 29 patients (52 per cent) had moderate or severe residual weakness.

Cases Reported by Kabat and Knapp.—Kabat and Knapp¹⁰ described the results obtained by the Kenny treatment with the administration of neostigmine. The authors based the justification of the use of neostigmine on the stretch reflex; they stated the belief that in persons with poliomyelitis the trigger mechanism is probably set at a lower level than normal. This seems a reasonable conception, and that such a lowered threshold could persist in muscles of most patients for months seems logical.

Was there any striking modification of the clinical conditions? After analyzing the data, it was difficult for us to conclude just what the condition of some patients was at the end of the period of observation.

The authors stated that in patient 4 there was no change in the triceps muscle (previously described as spastic) and then that the administration of neostigmine accelerated recovery. Phrases such as “stepped up recovery” and “accelerated recovery” are used despite the fact that none of the 20 patients were cured. All these terms are relative. There were no controls for comparison and all of the patients had some residual paralysis at the end of the period of observation.

We should classify case 5 in group 4 C. Recovery was good, though no mention was made as to whether the leg had recovered. It could hardly be admitted that in case 7 the fine degree of difference in mobility mentioned would be of much importance, since such differences occur from day to day. There was limitation of motion in case 8, although no paralysis was mentioned. From the descriptions we assume, however, that it probably was present in this case and in case 9.

It took patient 10 six weeks and patient 13 eight weeks to achieve the improvement which is claimed. One patient (case 19) resembled one of our patients, who still remained bedridden, though every treatment was tried.

10. Kabat, H., and Knapp, M. E.: Use of Prostigmine in Treatment of Poliomyelitis, *J. A. M. A.* **122**: 989-995 (Aug. 7) 1943.

We cannot understand what is meant by “considerable increase in active motion” in the report on case 2 or by the statement that “recovery appeared to be more rapid” in the report on case 3.

The authors stated that flexion deformities that had been present for six months disappeared completely within one hour after the injection of neostigmine. One could accept the fact that there was spasticity of muscles which would be a potential cause of an ultimate deformity, but it seems incredible that the recovery could be immediate if the deformity had already appeared. The evidence presented does not show an effect on recovery other than that which could have been obtained by the use of hot packs or any other early treatment. We should have wanted a consultation with a neurologist in case 3, but for the record we accept the conclusions of the authors.

TABLE 4.—Classification of Kabat and Knapp's Patients Treated by the Kenny Method and with Prostigmine

Status				Status			
No.	Group	Before	After	No.	Group	Before	After
1	5 B	III	I	11	5 B	II	II A
2	5 B	III	III B	12	5 B	III	III A
3	5 B	III	III A	13	5 B	V	IV
4	5 B	IV	IV B	14	5 B	IV	IV A
5	5 B	IV	IV C	15	5 B	IV	IV B
6	5 B	IV	IV C	16	5 B	IV	IV B
7	5 B	III	II B	17	5 B	III	III A
8	5 B	III	II A	18	5 B	V	IV
9	5 B	III	II A	19	5 B	V	V
10	5 B	III	III A	20	5 B	III	III

Evidence that hypertonus or muscular spasm was decreased is indefinite. It is not our impression that Kabat and Knapp demonstrated that an effect was obtained by the use of neostigmine.

There were 20 patients, all of whom were in group 5 B and hence were considered in the analysis. None were completely cured. Three patients (15 per cent) advanced one status. Of the 17 patients who did not advance one status, 8 (46.4 per cent) improved to substatus A, 5 (29.4 per cent) improved to substatus B and 2 (11.7 per cent) improved to substatus C. Two patients (11.7 per cent) showed no improvement.

Analyzing the data by groups and statuses we find the following distribution:

Classification Before Treatment		Number of Patients	Classification After Treatment	
Group	Status		Group	Status
5 B	II	1		II A
	III	1		II
		6		III A
		2		III B
		1		III
	IV	1		IV A
		3		IV B
		2		IV C
	V	2		IV
		1		V

Cases Reported by Kenny.—Kenny¹¹ refers to 84 patients treated by her method but gives no details to support the statements and conclusions made.

ORTHODOX TREATMENT

In a recent epidemic in Canada, of 167 patients for whom the orthodox method of treatment was used, 82.2 per cent recovered normal or almost normal function. In the 1941 epidemic in Alabama, of 120 patients treated in the same way, 80 per cent were normal or practically normal.¹²

Cases Reported by Lenhard.—Lenhard described the results obtained by him during the epidemic which occurred in Maryland in 1941.¹³ He stated that in the treatment of his patients rest of paralyzed muscles was emphasized but that rest did not constitute complete immobilization. However, the statement that "rest did not constitute complete immobilization" is not clear in the light of the next statement to the effect that the extremities were supported in plaster shells, wire splints or braces which allowed relaxation of weaker muscles. Our interpretation was that the patient was not put in a cast with the muscles in a neutral position and then forgotten but that he was put in some contrivance that rested him but at the same time allowed frequent movement and early application of physical therapy. The patient's body was flexed slightly in bed or on a curved frame to prevent stretching of the abdominal muscles. Radiant heat was used for the stimulation of circulation, and massage was given as soon as soreness had disappeared. Passive movement of joints was carried out in a restricted range in direct ratio to the amount of muscular weakness. Exercises, consisting of assistive motion, were begun early, and their extent was increased as the muscles showed recovery. Other than the early use of appliances, the treatment was not unlike ours.

The statistics are interesting; the results were excellent and the report was well prepared. However, it is impossible to make definite comparisons of therapy, because the status of the patients before treatment is not described. It is our guess, however, that the results were as good as any reported. Lenhard's patients with "no

paralysis" probably correspond to our nonparalytic group; this group constitutes 18 per cent of his series and 19 per cent of ours. Ninety-six of Lenhard's patients (34 per cent) recovered completely, as compared with 39.7 per cent of ours. Forty-seven patients (16 per cent) were probably normal; 40 (14 per cent) had slight residual weakness; 32 (11 per cent) had moderate residual weakness; 14 (5 per cent) had great residual weakness, and 5 (2 per cent) had complete residual weakness. Of his 296 patients 9 (3.0 per cent) died. Seventeen (7.5 per cent) of our patients died.

The author presents a chart showing the number of times the muscles were examined and the results. His key to the grading of muscular function emphasizes the proper points. The rating of 95 to 100 per cent corresponds to our "completely normal," 70 to 90 per cent to status II, 40 to 60 per cent to status III, 10 to 40 per cent to status IV and 0 to 10 per cent to status V. We might not agree with him as to what constituted "complete" recovery and normal muscular function. We believe that a patient who requires stabilization has more than merely "slight residual weakness," since we infer that he had a permanent complication, perhaps even an ankylosing deformity. Unfortunately, the initial conditions of the patients were not described. Two per cent of the patients had complete residual weakness; that is, they were confined to wheel chairs. The incidence is almost the same as in our series (1.7 per cent).

Lenhard proves that the type of immobilization employed by him does not harm the patient. We agree with his conclusion that muscles do not improve in direct ratio to the degree of initial weakness and that they may continue to improve for eighteen months or more when patients are treated immediately after the onset of poliomyelitis. We agree also that even in patients seen a long time after the disease has started the muscles may improve if treated. Lenhard was aware that some patients get well spontaneously, but he made no mention of the fact.

Evaluation of the strength of individual muscles when divorced from the condition of the patient as a whole does not reveal information of value in judging results. However, such an analysis would probably be more valuable if the relative times of recovery of the various muscles could be compared.

Cases Reported by McCarroll and Crego.—McCarroll and Crego¹⁴ reported on 245 patients

11. Kenny, E.: *Infantile Paralysis: Importance of Treatment in the Acute Stage*, New York State J. Med. **42**:1645 (Sept. 1) 1942.

12. Key, J. A.: *Kenny Versus Orthodox Treatment of Anterior Poliomyelitis*, Surgery **14**:20-31 (July) 1943.

13. Lenhard, R. E.: *Results of Poliomyelitis in Baltimore*, J. Bone & Joint Surg. **25**:132-141 (Jan.) 1943.

14. McCarroll, H. R., and Crego, C. H., Jr.: *Evaluation of Physiotherapy in Early Treatment of Anterior Poliomyelitis*, J. Bone & Joint Surg. **23**:851-861 (Oct.) 1941.

treated from 1935 to 1941 inclusive. The total number of extremities involved was 487. We were unable to determine the initial condition of the patients and hence could not classify them for comparison.

McCarroll and Crego took patients after the contagious or acute stage of the infection was over and treated only those who were frankly paretic or paralyzed. They did not bolster their statistics of recovery with cases of nonparalytic, abortive and bulbar poliomyelitis.

Twenty-seven per cent of the extremities with initial complete or partial paralysis recovered normal function. What this would mean in terms of the patient as a whole is unknown; if anywhere near 27 per cent of the patients made complete recoveries, the results would be as good as any reported in the literature.

McCarroll and Crego stated that the initial paralysis of poliomyelitis may be due to blockage of the pyramidal tracts by localized edema or related conditions, without destruction of ganglion cells. The statement is interesting and intriguing, and the mechanism suggested is perhaps not impossible; but one wonders about the qualifying phrase "without destruction of ganglion cells." If cells of the anterior horn were not destroyed, there would be no paralysis. If the hypothesis were correct, there would be only disturbance of reciprocal innervation and spasticity. Probably the authors meant that horn cells might be simultaneously edematous and that a condition similar to spinal block was present. It is certain that pathologic changes may be found throughout the spinal cord, changes which do not parallel the symptoms.

One must agree with the authors when they state that physical therapy may not be the answer to all the problems in this disease and that control will probably be accomplished through prevention.

Report by Key.—Key¹² recently considered the points for and against the orthodox treatment and the Kenny treatment of poliomyelitis. The author described orthodox treatment as the application of splints or casts, which are removed twice daily, and the passive, not active, movement of the major joints through an arc of tolerance, pain being the brake. Splints are used only when needed, not in all cases or on all extremities.

Key used warm salt baths, hot packs or dry heat to induce vascular dilatation and started massage and training of muscles when tenderness disappeared. The patients were examined

monthly, and Key noted that this is a necessity because occasional paralysis of certain muscles may be missed and become evident only as time goes on. He corrected contraction by gradual stretching during the convalescent stage, and he stated that this condition does not recur. Our experience with stretching has been similar in most instances, although we have had failures.

Key mentioned variations of the orthodox method, such as under-water therapy, employed at Warm Springs, Ga., or prolonged splinting, as advocated by the Kendalls. He employed careful training of muscles. When plaster casts were applied for a few weeks, he removed them two or three times daily. He kept the patients absolutely quiet for a few days during the febrile stage. We agree that under the guidance of a properly trained person such methods will achieve good results, but we believe that no harm is done to the patient when casts are left on for a few weeks and then removed and physical therapy started. We do not believe that it has been proved definitely that such procedures do not constitute good treatment, or that the ultimate results would not have been the same were some other method followed. Our procedure would vary in only one detail. From our experience in treating poliomyelitis for over twenty years, we know that fixed casts unnecessarily applied, especially if allowed to remain too long, are harmful. In instances in which Key would probably immobilize with splints; we should use sandbags, which in truth are also splints.

Key stated that the Kenny method does not protect paralyzed muscles from stretching while the orthodox method does, and he denied the claim that the Kenny treatment prevents or lessens paralysis. He added that the lay press credits the Kenny method with remarkable cures and makes extravagant promises of cures. Physicians must avoid publicity and are more guarded in their prognoses. A physician has to prove his statements before a critical audience of persons who know something about the disease.

Key also stated (1) that deformities do occur in patients treated by the Kenny method, (2) that many patients treated by the Kenny method will be handicapped because of the lack of splints which would enable them to use their paralyzed limbs more efficiently, (3) that the Kenny treatment is laborious and messy and demands a relatively large number of specially trained technicians for a given number of patients and (4) that the Kenny method is rigid and cannot be used effectively in an epidemic of any magnitude.

He pointed out that the orthodox treatment is elastic and has weathered many epidemics and that poliomyelitis is an epidemic disease.

Cases Reported by Sherman.—Sherman¹⁵ described the results of treatment at the University of Chicago of 70 patients during the epidemic of 1943. The patients were given supportive therapy only, and the disease was allowed to run its natural course. The results were excellent. Unfortunately, exact comparisons cannot be made, since the condition of the patients was not described.

TREATMENT WITH VITAMINS AND ARTIFICIAL FEVER

Cases Reported by Stone.—To treat infantile paralysis Stone¹⁶ used a combination of artificial fever, thiamine hydrochloride and vitamins B and E. He administered the thiamine intravenously or intramuscularly during the height of the fever. The average number of treatments was four, although 1 child received seven intramuscular and four intraspinal doses. As the patients progressed vitamin B complex and vitamin E were given orally.

TABLE 5.—Classification of Stone's Patients Treated with Artificial Fever and Vitamins

No.	Group	Status		No.	Group	Status	
		Before	After			Before	After
1	5 B	III	III C	7	5 B	IV	III
2	5 B	III	III C	8	5 E	III	III C
3	5 B	III	III C	9	5 B	V	I
4	5 B	III	III C	10	5 E	III	I
5	5 B	III	III C	11	5 E	III	III C
6	5 D beta	III	III C				

The exact meaning of the term "fibrosis" used by Stone in his report on cases 9 and 11 is not clear. It is probably an error, for it is difficult to understand how the patient could recover if general fibrosis, which implies destruction of parenchymatous tissue with replacement by connective tissue, had been present. It may be, however, that there was so much hypertrophy of the remaining muscular tissue that the previously prominent fibrosis was obscured.

The patients treated by Stone were of the type about which physicians want to know more; that is, they all had obvious paralysis.

15. Sherman, M. S.: The Natural Course of Poliomyelitis, J. A. M. A. **125**:99 (May 13) 1944.

16. Stone, S.: Artificial Fever and Vitamin Therapy in Treatment of Anterior Poliomyelitis: Report on Intraspinal Administration of Thiamine Chloride Combined with Artificial Fever Therapy, Arch. Phys. Therapy **24**:350-361 (June) 1943.

All of Stone's 11 patients are considered in this analysis since ten were in group 5B and 1 in group 5D beta. Two patients (18.1 per cent) were completely cured. One patient (9.1 per cent) advanced one status, making 3 (27.2 per cent) who advanced at least one status. The 8 patients who did not advance one status improved to substatus C.

Analyzing the data by groups and statuses, we find the following distribution:

Classification Before Treatment		Number of Patients	Classification After Treatment, Status
Groups	Status		
5 B	III	1	I
		7	III C
	IV	1	III
	V	1	I
5 D beta	III	1	III C

COMMENT

Table 6 was constructed from the data in six recent reports in the literature to present a comparison of the results. The statistics for the Toomey-Feiss method were derived from our series of 226 cases in the 1941 epidemic.¹

The percentages of patients who recovered completely after treatment with the Toomey-Feiss, the Pohl-Kenny and the Stone method were about equal.

Advances of one or more statuses were made by 23.8 per cent of the patients treated by the Pohl-Kenny method, 19.5 per cent of our patients, 14.3 per cent of Daly's patients and 15 per cent of Kabat and Knapp's. The patients who advanced one or more statuses plus those who were cured constituted 40.5 per cent of our series (Toomey-Kohn), 47.6 per cent of the group treated by the Pohl-Kenny method, 19 per cent of Daly's series and 27.2 per cent of Stone's.

Only 12.2 per cent of our patients improved to condition A; 36.3 per cent of the patients receiving the Pohl-Kenny treatment and 46.4 per cent of those treated by Kabat and Knapp reached condition A. Such minor improvements, however, may be merely a question of personal opinion and equation, improvement no matter how slight having been included.

The advance to substatus B, which is determined on the basis of positive objective evidence, was achieved by 36.6 per cent of our patients, 36.3 per cent of Pohl's, 17.6 per cent of Daly's patients treated by the orthodox method, 64.9 per cent of Daly's patients treated by the Kenny method and 29.4 per cent of Kabat and Knapp's series. Improvement to condition C was achieved by 37.8 per cent of our patients, 27.4 per cent of the Pohl-Kenny series, 11.8 per cent of Daly's control series, 11.7 per cent of the Daly-

Kenny series, 11.7 per cent of the Kabat-Knapp series, and 100 per cent of Stone's series.

The incidence of advancement to substatus B in Daly's series (64.9 per cent) seemed relatively higher until we noticed that the percentage for statuses B and C considered together is 76 in their series as compared to 74 in ours. On the

Kabat and Knapp's and 11 in Stone's. Regarding the data for all the patients who did require treatment, especially those with a paralytic poliomyelitis, those with so-called spasm and nothing else, we have used as basis of comparison 138 of our cases, 21 Pohl's, 18 of Daly's first series (orthodox

TABLE 6.—*Comparison of the Results in Groups Treated by Various Methods*

	Toomey- Feiss	Pohl- Kenny	Daly Orthodox	Daly- Kenny	Kabat- Knapp	Stone
Patients completely cured, per cent.....	21.0	23.8	0	4.7	0	18.1
Patients advanced one or more statuses, per cent.....	19.5	23.8	5.5	14.3	15.0	9.1
Patients advanced one or more statuses or cured, per cent.....	40.5	47.6	5.5	19.0	15.0	27.2
Patients improved to condition A, per cent.....	12.2	36.3	17.6	23.4	46.4	0
Patients improved to condition B, per cent.....	36.6	36.3	17.6	64.9	29.4	0
Patients improved to condition C, per cent.....	37.8	27.4	11.8	11.7	11.7	100.0
Patients not improved, per cent.....	0	0	52.8	0	11.7	0
Number of patients in series	226	26	43	28	20	11
Number of patients considered in evaluation of treatment	138	21	18	21	20	11
Deaths in entire group, per cent.....	7.5	0	0	0	0	0
Patients completely cured, including those with nonparalytic poliomyelitis and those in groups 5 D alpha and 5 E gamma, per cent.....	40.6	38.4	7.1	10.7	0	18.1

other hand, patients in condition C were practically cured, and in this category there were only 11.7 per cent of Daly's group as compared to 37.8 per cent of ours and 27.4 per cent of Pohl's.

The numbers of cases analyzed in the various series were 226 in ours (Toomey and Kohn), 26 in Pohl's (Kenny), 43 in one of Daly's (orthodox) and 28 in the other (Kenny), 20 in

21 of Daly's second series (Kenny), 21 of Kabat and Knapp's and 11 of Stone's.

If patients with nonparalytic and bulbar poliomyelitis are included, recovery was complete 40.6 per cent of our patients, 38.4 per cent Pohl's, 7.1 per cent of Daly's first series (orthodox), 10.7 per cent of Daly's second series (Kenny) and 18.1 per cent of Stone's and none of Kabat's patients.

Obituaries

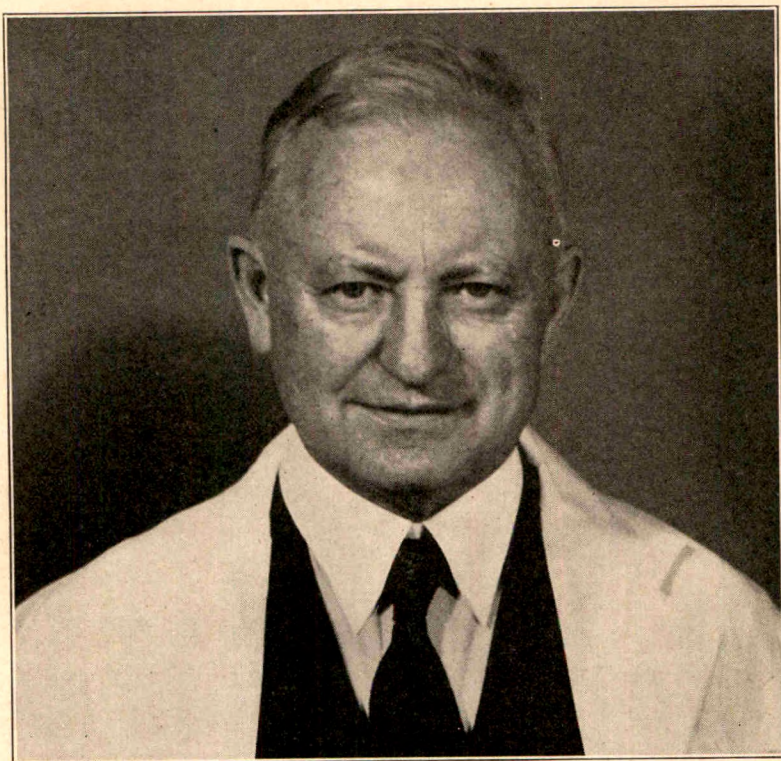
FREDERIC WILLIAM SCHLUTZ, MD.

1880-1944

Frederic William Schlutz, chairman of the department of pediatrics of the University of Chicago, died on March 8, 1944, at the age of 63. His father's family came from Frankfort on the Main, Germany. His grandfather came to the United States in the early part of the last century because of his desire for political freedom.

appointed professor of pediatrics at Minnesota, and in 1930 he was called to the University of Chicago as head of the new Children's Hospital, which was opened at that time. He continued in full service in his specialty until his death.

He was elected to the American Pediatric Society in 1917 and was one of the recognized



FREDERIC WILLIAM SCHLUTZ, M.D.

1880-1944

Dr. Schlutz was born in Greene, Iowa, and educated at Wartburg College, Clinton, Iowa, and the University of Maryland Medical School. He entered practice at the Mining Hospital in Eveleth, Minn. After some years he decided to enter the field of children's diseases. To train himself for this specialty he went to Europe in 1909. Most of his work was done in Berlin under Professors Czerny and Finkelstein. In 1910 he returned to the United States and joined the faculty of the University of Minnesota as instructor in biochemistry and in pediatrics. In 1913 he returned again to Europe. He steadily advanced in his chosen field. In 1924 he was

leaders of his profession in the United States. In 1927 he visited many of the countries of South America and there formed associations which continued, and which grew, throughout his life. He was a member of the White House Conference on Child Health and a member of the Pan-American Committee. It was planned in 1943 that he should go again to South America, as a representative of the United States Department of State, and there for a period of four or five months conduct a series of lectures and teaching clinics.

Dr. Schlutz was a man of great industry. The main interest in his life was his chosen pro-

fession. While in Minneapolis he soon found that he had developed an enormous practice in the diseases of children. The activity in Minnesota which gave him the greatest personal satisfaction was the establishment and development of the Infant Welfare Society in that city.

When he came to the University of Chicago he left the restrictions of an exacting practice to become a member of the full time teaching staff. This gave him freedom for research, and his steady interest in biochemistry led him into a series of investigations which were essentially chemical. Later, this developed into an extensive program directed toward investigation of physical fatigue in young people.

Throughout his life Dr. Schlutz had a driving energy. This quality, coupled with his inheritance from his Hessian ancestors, made him fight always for what he believed to be right. He was a kindly and generous man and was always eager to assist and to stimulate his students and associates. It was this quality that made him active and successful in promoting friendly relationships between the members of the medical profession in the United States and in South America. He was an unusually versatile linguist and a great student of history. His passing has left many friends in the United States, in Europe and in South America with a deep sense of personal loss.

D. B.

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

EFFECT OF HYPOGLYCEMIA AND ANOXIA ON THE SURVIVAL PERIOD OF INFANT AND ADULT RATS AND CATS. HAROLD E. HIMWICH, JOSEPH F. FAZEKAS and EDMUND HOMBURGER, *Endocrinology* **33**:96 (Aug.) 1943.

It has been found in general that newborn animals, of all species examined, possess greater resistance to anoxia than adults, a resistance dependent on the greater capacity of the infant brain to withstand deprivation of oxygen. Because dextrose, like oxygen, is necessary to cerebral metabolism, the experiments here reported were devised to test the relative capacity of infants and adults for resisting hypoglycemia.

It is concluded that infant rats survive hypoglycemia longer than adults. The factor determining the difference in the survival period is the ability to maintain the function of the brain during hypoglycemia. This capacity of the infant brain to endure hypoglycemia is associated with its lower cerebral metabolic requirements.

The survival period of the anoxic infant, but not of the anoxic adult, is prolonged by hyperglycemia. The adult cannot obtain sufficient energy from glycolysis to sustain the higher rate of cerebral metabolism. Hypoglycemia, however, shortens the survival period of anoxia for both infant and adult rats.

JACOBSEN, Buffalo.

THE INTERRELATIONS OF SERUM LIPIDS IN NORMAL PERSONS. JOHN P. PETERS and EVELYN B. MAN, *J. Clin. Investigation* **22**:707 (Sept.) 1943.

An analysis has been made of a large number of measurements of the lipids in the serum of normal persons in the postabsorptive state. In most instances cholesterol, lipid phosphorus and total fatty acids were measured, which permitted the estimation of free fat by difference. On a few occasions cholesterol partitions were carried out, and more rarely iodine numbers were determined.

The range of variation of all lipid fractions in the whole series was great: from 107 to 320 mg. per hundred cubic centimeters for cholesterol, from 6.1 to 14.5 mg. per hundred cubic centimeters for lipid phosphorus and from 0 to 17.8 milliequivalents per liter for fatty acids of free fat; free fat varied most and lipid phosphorus least. There is no distinction between the serum lipids of normal men and women. The serum lipids of obese adults and children are indistinguishable from those of normally nourished persons.

The ratio of cholesterol to lipid phosphorus is more constant than either of the functions of which it is composed. The standard deviation of this ratio from its mean in this series was only ± 12 per cent. The ratio tends to vary also directly with the concentration of cholesterol.

The ratio of free to total cholesterol is as constant in this series as it has been reported by previous observers, varying only from 0.24 to 0.32 with an average of 0.28.

The concentration of free fat in the serum is not definitely correlated with that of either cholesterol or lipid phosphorus.

A study of the course and the interrelationships of the lipids in disease should be more informative than single observations of any one of the lipid components.

FROM THE AUTHORS' SUMMARY.

THE EFFECT OF SODIUM CHLORIDE UPON THE DISPOSITION OF INJECTED GLUCOSE IN A STRAIN OF RATS. GEORGE SAYERS, MARION SAYERS and JAMES M. ORTEN, *J. Nutrition* **26**:139 (Aug.) 1943.

The effect of sodium chloride on the disposition of intraperitoneally injected dextrose was studied in a strain of rats having a low tolerance for dextrose. The use of an 0.85 per cent solution of sodium chloride as an injection medium for the sugar improved the tolerance of these rats, but neither the peritoneal absorption nor the renal excretion of dextrose was affected. The administration of sodium chloride with dextrose favored the deposition of glycogen in both the liver and the rest of the body and simultaneously decreased the "free" sugar in the blood and tissues. The oxidation and conversion to fat of the dextrose appeared to be decreased to a normal level. The sodium chloride improved the low tolerance to dextrose in this strain of rats by increasing the storage of the administered sugar as glycogen.

FREDEEN, Kansas City, Mo.

DIGESTIBILITY OF CERTAIN HIGHER SATURATED FATTY ACIDS AND TRIGLYCERIDES. RALPH HOAGLAND and GEORGE G. SNIDER, *J. Nutrition* **26**:219 (Sept.) 1943.

Mature male rats were used in these experiments to determine the digestibility of pure stearic, palmitic, myristic and lauric acids and of the corresponding triglycerides. Each fatty acid was mixed in the proportions of 5, 10, 15 and 25 per cent with pure olive oil and each triglyceride in proportions of 5 and 10 per cent. The mixture of fatty acid and olive oil constituted 5 per cent of the diet. The approximate digestive coefficients of stearic acid, which was poorly absorbed at all levels of intake, ranged from 9.4 to 21 per cent. The coefficients for palmitic acid ranged from 23.8 to 39.6 per cent; for myristic and lauric acids the coefficient was practically 100 per cent when the fat mixtures contained 5, 10 or 15 per cent of either acid, but somewhat lower when the mixture contained 25 per cent of the acid. Glyceryl tristearate was poorly utilized; glyceryl tripalmitate was much more digestible than the tristearate; the digestive coefficients were 6 to 8 per cent, and 84 to 82 per cent respectively when the mixtures contained 5 and 10 per cent of the triglyceride. Glyceryl trimyristate and trilaurate were thoroughly absorbed.

FREDEEN, Kansas City, Mo.

DIETARY REQUIREMENTS FOR FERTILITY AND LACTATION. BARNETT SURE, *J. Nutrition* **26**:275 (Sept.) 1943.

Lactation in the albino rat was favorably influenced to a considerable extent when paraaminobenzoic acid was given. Inositol had a pronounced injurious influence on lactation, which was counteracted by paraaminobenzoic acid.

FREDEEN, Kansas City, Mo.

STREAMLINED INFANT FEEDING. NORMAN W. CLEIN, J. *Pediat.* **23**:224 (Aug.) 1943.

This report is based on a study of about 3,000 infants over a period of twelve years. The object is to show that most infants at the age of 5 or 6 months can be placed on a schedule of three meals a day. The evaluation of the efficacy of this method of feeding is based primarily on the infant's own tolerance for the diet. His reactions are the sole basis for judgment of the amount of food he requires.

The number of ounces at each feeding is determined by the baby, so that he receives as much as he requires of the formula within a period of about twenty minutes. If the baby receives more and richer foods at a feeding, it is not necessary to feed him so often.

The rate of growth and development of the infant is the chief criterion as to the amount and number of feedings he requires. The age of the infant is of minor importance. The individual development of each infant is also the deciding factor as to when to begin solid foods. Solid foods are added at the following approximate weights: When the infant weighs 10 pounds (4.5 Kg.) add banana and apple sauce; 10 (4.5 Kg.) to 12 pounds (5.4 Kg.), cereals; 12 (5.4 Kg.) to 14 pounds (6.4 Kg.), vegetables and soups; 12 (5.4 Kg.) to 16 pounds (7.3 Kg.), fruits, and 16 (7.3 Kg.) to 18 pounds (8.2 Kg.), meat, fish and cottage cheese. Hard foods, such as toast and bones, are added at the age of 5 to 6 months, as soon as the baby is able to hold things in his hands. All food for a child 6 months old is mashed with a fork (not pureed), whether the infant has teeth or not. Whole, fresh, pasteurized milk is usually added to the diet when the infant weighs 16 pounds (7.3 Kg.) or over.

In the cases analyzed the average age at which a schedule of only four feedings was instituted was 3.1 months, and the average weight at that time was 12.7 pounds (5.8 Kg.). The average weight when the schedule was reduced to three feedings was 18 pounds (8.2 Kg.) and the average age 5.75 months. The average weight at one year was 23.41 pounds (10.6 Kg.) and the average height 30 inches. In a group of 100 babies whose cases were studied in detail, there was less than one infection of the upper respiratory tract to each infant for the entire year and no infections or colds in 43 of the infants. There were only 2 cases of real anorexia. This is the chief reason why fewer feedings are advisable; appetite is created by hunger. An infant can eat larger quantities of food when the intervals between feedings are longer; therefore there is much less anorexia when babies are fed according to this system. There was very little vomiting. Over-eating did not occur, as infants will usually stop eating when satisfied. Only 8 infants had diarrhea of a minor degree. Nine had cutaneous eruptions, mild eczemas, which were attributed to food.

The indications for instituting a schedule of four feedings are as follows: (a) The weight approaches 10 to 12 pounds (4.5 to 5.4 Kg.), or the age is 3 to 4 months, with weight less than 12 pounds (5.4 Kg.). (b) The baby has to be awakened for the 10 p. m. feeding. (c) The infant takes large amounts of "formula" at a time. (d) Cereals and fruits are added to the diet.

The schedule of three meals a day is instituted: (a) When the infant weighs about 17 or 18 pounds (7.7 to 8.2 Kg.), or is 5 or 6 months of age and weighs less than 17 pounds (7.7 Kg.). (b) When he sleeps past his 6 a. m. feeding, or does not require much at his 2 p. m. feeding. (c) When the infant is receiving cereal,

vegetables and fruit in addition to milk. This schedule is also used for small babies who do not require large amounts of food.

The diets should consist of formulas composed of either fresh or canned milk, water and table sugar. Any of the cooked or precooked cereals are used; a fruits and vegetables available to other members of the family are given the infants. No specially prepared foods of any kind are required. Sterilization of bottle and nipples is discontinued when the child is 4 months of age and begins to put his hand and other objects in his mouth. Vitamin D in the form of cod liver oil or vitamin concentrates is added at one month of age. No synthetic vitamin C is required, as the infant receives the natural vitamins in his food to supply the normal requirements.

The infant is just another member of the family and is made to fit into the family routine as much as possible. The mother enjoys her infant much more because she has more time to be with him, as there is much less work for her to do. SHMIGELSKY, Chicago.

WHOLE LACTIC ACID EVAPORATED MILK DOES NOT REQUIRE A REFRIGERATOR. HARVEY G. TAYLOR and ROBERT W. ROBBETS JR., J. *Pediat.* **23**:307 (Sept.) 1943.

Evaporated whole milk with lactic acid added can be left in open dishes at room temperature for three days before molds are evident and for five days before bacteria appear. As the amount of prepared formula made from the usual 13 ounce can of evaporated milk is always consumed within forty-eight hours, refrigeration is unnecessary. The incidence of diarrhea, vomiting and bacillary dysentery is lower in infants fed evaporated whole lactic acid milk than in infants who receive any other food. The process of evaporation removes the risk of the diseases which can be spread through dairies.

"The contents of a 13 ounce (390 cc.) can of unsweetened evaporated milk are poured into a quart jar, previously 'scalded' with boiling water, and the empty can nearly filled with boiling water, in which then are dissolved 1 teaspoon of lactic acid (U. S. P.) and 2 level tablespoons of sugar. As soon as this solution is cold, it is poured slowly into the quart jar containing the unsweetened evaporated milk while shaking the jar constantly. Although not necessary, it is advisable, in order for the lactic acid to accomplish its full bactericidal effect, that the mixture be kept six hours before being fed in required amounts to the infant. It should not be boiled or pasteurized as it will curdle. Infants of any age can be fed 100 cc. (100 calories) of this mixture per kilogram of body weight (1½ ounces, 45 calories, per pound) in twenty-four hours, divided into four to six feedings. If a child requires more than this amount (one can each of milk and water, a total of 780 cc., 26 ounces), he also needs solid food."

SONTAG, Yellow Springs, Ohio.

THE USE OF CEREAL-THICKENED FORMULAS TO PROMOTE MATERNAL NURSING. CHESTER A. STEWART, J. *Pediat.* **23**:310 (Sept.) 1943.

Complemental feedings by bottle favor the early discontinuance of maternal nursing, whereas the consumption of semisolid foods usually does not diminish the vigor with which infants nurse. This special superiority of foods of moderately thick consistency over liquid mixtures was tested thoroughly over a period of several years. The author's experience with this special method of feeding is exemplified by the records of a

ected group of 51 infants who were breast fed for eight months and who also received from the third day life a moderately thick preparation composed of real cooked in equal parts of whole cow's milk and water, with 5 per cent of sucrose and a pinch of salt added.

At the conclusion of the first month of life the diet of this selected group of infants included mother's milk, farina or oatmeal cooked in milk, sucrose and orange juice. Between the ages of 4 and 8 weeks cod liver oil, codrines in oil, creamed tuna fish, salmon and shrimp as well as crushed, unstrained carrots and canned peas were added to the diet. Subsequent additions resulted in the construction of a liberal diet for these infants in the first year of life. This regimen promoted satisfactory gains in weight, and its use was accompanied by a continuance of maternal nursing in each instance. A program devised to compensate for deficits in the supply of mother's milk without resorting to bottle feedings provided for the following additions to the diet: real-thickened formula, orange juice and cod liver oil in the first month; mashed ripe banana and creamed tomato in the second month; boiled egg yolk, crushed strained carrots and peas, applesauce, prune pulp and orange juice in the third month; sea fish, whole egg, potato and other vegetables in the fourth month and meats in the fifth month.

Experience with this program in the South for eighteen months indicates that a warm climate is no contraindication to its use.

In conclusion, the routine use of formulas thickened with cereal, fed by spoon to young infants for the purpose of compensating for varying degrees of deficiency in the supply of breast milk is recommended. This alternative for complementary feeding by bottle does not scourage the continuance of maternal nursing.

The introduction of a wide variety of appropriate, moderately coarse, semisolid foods into the diet at an early age acquaints young infants with the majority of the important flavors, aromas and food textures they are apt to encounter during life, and this early experience promotes excellent eating habits which tend to persist. The liberal diet also safeguards nutrition by providing multiple, overlapping sources of essential nutrients.

SHMIGELSKY, Chicago.

MILK INTOLERANCE, THE CAUSE OF A NUTRITIONAL ENTITY. P. A. McLENDON and D. S. JAEGER, South. M. J. **36**:571 (Aug.) 1943.

The authors pointed out that the medical profession as long advocated milk as the ideal food for infants and children. Arguments are no longer needed to induce people to drink milk, for nutritionists, dentists and the dairy interests have furthered the cause. Nevertheless, it is the physician's duty to protect the "intolerant minority"; he must be able to recognize members of this minority and free them from the dictum of "a quart of milk a day."

The management of these patients becomes a relatively simple problem after the diagnosis is made and the mother is convinced that milk can be safely eliminated. McLendon and Jaeger gave some of these patients calcium, iron or extra vitamins. These accessories were not usually more than the child was already taking or had taken at some previous time, and the authors feel sure that the supplements played a minor role in the rapid improvement which followed the elimination of milk.

SCHLUTZ, Chicago.

Vitamins; Avitaminoses

VARIATIONS IN THE CUTANEOUS MANIFESTATIONS OF VITAMIN A DEFICIENCY FROM INFANCY TO PUBERTY. CHESTER B. FRAZIER, CH'UAN-K'UEI HU and FU-T'ANG CHU, Arch. Dermat. & Syph. **48**:1 (July) 1943.

The authors report the observations on 6 patients with vitamin A deficiency. They conclude that progressive development of follicular hyperkeratosis of the skin is correlated with the age of the subject. In infants and in children of prepubertal age such lesions occur infrequently, and the younger the child the milder the degree of follicular damage.

The earliest clinical sign of cutaneous involvement was simple xerosis of the superficial epithelium. This was accompanied by histologic evidence of keratotic changes in the epithelium of some of the hair follicles. Other follicles seemed to have escaped damage as judged by the absence of structural abnormalities.

An atrophic stage, characterized by thinning of the epidermis, was observed in the skin of the youngest patients, who presented only cutaneous xerosis. In pubertal and adolescent patients the follicular lesions attained the greatest magnitude.

The pathologic changes in the pilosebaceous structures were so correlated with the age of the patient as to suggest that the state of sexual development was the critical factor conditioning the response of these structures to a deficiency of vitamin A.

JACKSON, Iowa City.

Prematurity and Congenital Deformities

SPINA BIFIDA AND CRANIUM BIFIDUM. FRANC D. INGRAHAM and H. WILLIAM SCOTT JR., New England J. Med. **229**:108 (July 15) 1943.

The Arnold-Chiari malformation is a congenital anomaly of the hindbrain characterized by downward elongation of the cerebellum and brain stem into the cervical portion of the bony spinal canal.

Twenty consecutive cases of Arnold-Chiari malformation that came under observation at the Children's Hospital from 1929 to 1943 were examined. Nineteen of these were studied at autopsy as well as clinically. All the patients were infants between 2 days and 18 months of age. Meningocele, with or without hydrocephalus, was the reason for hospitalization in each instance.

The majority of the patients had associated microgyria and craniola cunia.

GEGENBACH, Denver.

EFFECT OF WAR CONDITIONS ON THE PREMATURE INFANT. C. ELAINE FIELD, Lancet **2**:82 (July 17) 1943.

The rearing of 185 premature infants under adverse war conditions with the low mortality of 8.1 per cent is reported. Only 1 infant died of infection.

The high standard of experienced nursing, with minimum handling of the infants, is the explanation offered for the low mortality in this series. Breast milk was given to every infant, and the administration of thyroid was found helpful.

LANGMANN, New York.

Newborn

SKIN DISEASE OF THE NEWBORN INFANT. MACHTELD E. SANO, J. Pediat. **23**:280 (Sept.) 1943.

As a result of an intensive study of a case of desquamative erythroderma (Leiner's disease) correlated

with an extensive review of the literature, the author concludes that the underlying cause of desquamative erythroderma (Leiner's disease) and exfoliative dermatitis (Ritter's disease) is a temporary dysfunction of the endocrine system. The dysfunction in the majority of infants probably originates in the mother, who has to adapt herself physiologically to the demands put on her endocrine system during pregnancy.

The histologic examination of the endocrine glands, illustrated by photomicrographs, and biochemical studies of the case confirm some of the observations reported in the literature.

The conditions observed in this detailed clinical and histopathologic study indicate that desquamative erythroderma cannot be considered as an entity but rather as a manifestation of an underlying cause responsible also for exfoliative dermatitis and possibly other cutaneous diseases in the newborn infant.

SONTAG, Yellow Springs, Ohio.

PRACTICAL APPLICATIONS OF A ROUTINE BLOOD COUNT IN THE NEWBORN. FRANK C. NEFF, Minnesota Med. 26:779 (Sept.) 1943.

The author emphasizes the fact that since the majority of infants are born in hospitals greater use of the laboratories should be made in determining the hemoglobin content and the blood count of the newborn babies. In fact, he recommends that it be made a routine measure and that if any abnormal change is found a transfusion or transfusions be given to the infant. A transfusion set is illustrated. With the apparatus described blood may be transfused into the small vessels of the scalp, wrist or ankle as well as into the veins of the neck, the elbow or the thigh. Even with a needle as small as a .25 gage it is usually possible to introduce citrated blood or plasma at the rate of 10 cc. per minute, thus only five to ten minutes being required for the amount needed in an infant.

STOESSER, Minneapolis.

THE FIRST MONTH OF LIFE: GENERAL SURVEY. CHARLES MCNEIL, Edinburgh M. J. 50:491 (Aug.) 1943.

The University of Edinburgh organized its pediatric department under the name of "Child Life and Health." Charles McNeil, professor in that department, discusses in this article deaths and their causes in the neonatal period. Less than 1 per cent of the natal deaths were due to infection, but 27 per cent of the deaths occurring in the neonatal period were due to this cause. The natural immunity of newborn babies is low, as is shown by the fact that staphylococcal infection of the skin spreads much more rapidly than in older children. Infection of the meninges and lungs with the colon bacillus is not uncommon in the first month of life, but it is rare afterward. The eye and the umbilical wound were commonly invaded formerly but rarely now, since an effort is made to protect such vulnerable regions. Thrush, benign in the mouth, is dangerous when it invades the esophagus.

McNeil concludes that newborn babies are vulnerable to infection and that congregation in nurseries favors cross infection. With increasing numbers of babies born in institutions, the dangers must be countered by a stricter nursing technic. In the years 1939 and 1940 the neonatal deaths at the Maternity Pavilion, Royal Infirmary, Edinburgh, numbered 256, one fourth of which were due to infection during the first month of life. Gastroenteritis was the most frequent cause and

pneumonia the second; 4 deaths from thrush of the esophagus occurred in premature infants.

The author summarizes the problems of the first month, which he regards as forming a link in the chain of maternal and child health. There will be a far reaching influence from a deeper understanding and better management of these problems.

NEFF, Kansas City, Mo.

Acute Contagious Diseases

OBSERVATIONS ON BACTERIAL ALLERGY IN SCARLET FEVER. JAMES A. CONNER and ALBERT MILZER Illinois M. J. 84:214 (Sept.) 1943.

Three patients in whom urticaria developed while they were convalescing from uncomplicated scarlet fever were tested with various preparations from the hemolytic streptococci isolated from their throats. Positive cutaneous reactions were constantly observed after the intradermal inoculation of suspensions of killed broth cultures and killed, washed saline suspensions, while heated and unheated Berkefeld filtrates, Dick toxin and human convalescent serum gave no reaction.

The possibility of bacterial allergy as a cause is presented, and the possible correlation of such allergy to delayed or late hemorrhagic nephritis and non-suppurative arthritis is considered.

BARBOUR, Peoria, Ill.

MENINGOCOCCEMIA. NELLES SILVERTHORNE, J. Pediat. 23:155 (Aug.) 1943.

The author reported 3 cases of meningococcemia without meningitis. In 2 cases the spinal fluid was clear and sterile and had a normal cell count. In the other case the fluid was not examined, as there were no signs of meningeal infection. None of the 3 patients were treated with any chemotherapeutic drug or serum, and all recovered. Laboratory studies showed that bactericidal power against the patient's own infecting strain of meningococcus developed in the whole blood of each patient, coincident with recovery; in 2 patients the strain was type II and in the other type I. Clinical evidence was presented which supports the contention that other factors than the type of therapy used are responsible for recovery from meningococcal infections.

SONTAG, Yellow Springs, Ohio.

POSTRUBELLA ENCEPHALOMYELITIS. FREDERICK J. MARCOLIS, JAMES L. WILSON and FRANKLIN H. TOPP, J. Pediat. 23:158 (Aug.) 1943.

Fourteen cases of postrubella encephalitis are reported, and the clinical features of these and of the 34 previously reported cases are analyzed. It is estimated that the incidence of this complication in the 1942 epidemic of rubella in Detroit was 1 in 6,000 cases.

There is nothing diagnostic about the course or symptoms of the condition except that it follows rubella within a week, at an average of four days after the rash appears. No laboratory tests or reactions are specific. The leukopenia of rubella becomes a leukocytosis with the onset of the encephalitis. The spinal fluid has a normal or slightly increased amount of sugar, an increased amount of globulin and a cell count between eight and five hundred, with an average of ninety-one.

Death occurred in 10 of the 48 cases. In only 2 of the surviving patients did neurologic sequelae develop. The disease causes death or allows complete recovery within three or four days. SONTAG, Yellow Springs, Ohio

EFFECTS OF POLIOMYELITIS VIRUS ON THE URINARY BLADDER OF RABBITS. JOHN A. TOOMEY, JAMES D. PILCHER and PHILLIP T. ROSSMAN, J. Pediat. **23**: 166 (Aug.) 1943.

Toomey and his associates report that they were unable to demonstrate that the virus of poliomyelitis or any combination of this virus with toxin obtained from the growth of colon bacilli could cause paralysis of the bladder of a rabbit when injected therein.

SONTAG, Yellow Springs, Ohio.

ATTEMPTS TO RECOVER POLIOMYELITIS VIRUS FROM FRUIT, WELL WATER, CHICKEN CORDS AND DOG STOOLS. JOHN A. TOOMEY, WILLIAM S. TAKACS and LINDA A. TISCHER, J. Pediat. **23**:168 (Aug.) 1943.

Attempts were made to recover poliomyelitis virus from fruit (washings), well water, stools from sick dogs and cords from paralyzed chickens found in vicinities where human poliomyelitis had occurred. Although the virus may have been present in the specimens tested, its existence could not be demonstrated when either the eastern cotton rat or the *Macaca mulatta* monkey was used as the test animal.

AUTHORS' SUMMARY.

ATTEMPTS TO ISOLATE POLIOMYELITIS VIRUS FROM URINE. JOHN A. TOOMEY, LINDA A. TISCHER and WILLIAM S. TAKACS, J. Pediat. **23**:172 (Aug.) 1943.

The presence of the specific virus of poliomyelitis was not demonstrated in urine obtained post mortem from the bladders of patients with poliomyelitis when the eastern cotton rat was used as the test animal.

AUTHORS' SUMMARY.

ACUTE INFECTIOUS MYELITIS FOLLOWING RUBELLA. MILTON H. MORRIS and ABNER ROBBINS, J. Pediat. **23**:365 (Sept.) 1943.

The occurrence of the syndrome of acute infectious neuritis or acute benign myelitis after rubella is uncommon. This is a report of a case of acute benign infectious myelitis in an 18 year old youth who had rubella two weeks prior to admission to the hospital. In the two week interim he felt well, attended school and played baseball. Two weeks after the onset of rubella, for which he remained in bed four days, he noticed weakness of his knees, and the following day he was unable to walk or to urinate. The essential physical conditions observed were those of an acutely ill, well nourished young man with bilateral cervical lymphadenopathy, a fine brownish desquamation over the skin and a large globular mass in the suprapubic region corresponding to the position of the bladder. Abdominal and cremasteric reflexes were absent, and the patellar and achilles reflexes were accentuated. No pathologic reflexes were elicited. Sensations of touch and pressure were exaggerated in the lower extremities. The white blood cell count was 17,600, with 92 per cent polymorphonuclear leukocytes. The urine was normal. The spinal fluid contained 22 cells per cubic millimeter, all lymphocytes; a smear revealed no organisms. The reaction for albumin was 1 plus; a trace of globulin was present, and 90.3 mg. of sugar and 728 mg. of chlorides per hundred cubic centimeters. The reaction of the spinal fluid with colloidal gold was negative, and a culture showed *Bacillus subtilis* (contamination). A second sample of spinal fluid had a 2 plus content of albumin and a trace of globulin and the total protein content was 62.5 mg. per hundred cubic centimeters.

Examination of the eyes revealed no abnormality. The temperature remained elevated, 103 F., for the first three days. It was necessary to catheterize the patient for one week. His inability to walk gradually diminished from the eighth day, and at discharge, two weeks after admission to the hospital, he could walk with support. The paresthesias almost disappeared, and the patellar and achilles reflexes returned to normal, but the cremasteric and abdominal reflexes were still absent. Four weeks later all the symptoms disappeared except absence of the deep reflexes.

There are three views as to the possible cause of this disturbance. One view attributes it to the action of the virus of rubella, another to an allergic or anaphylactic phenomenon and a third to an unknown virus or toxin which is enabled by the presence of rubella to attack the nervous system.

SHMIGELSKY, Chicago.

ACUTE APPENDICITIS IN PATIENTS WITH THE COMMON CONTAGIOUS DISEASES. MAX GOODMAN and IRVING SILVERMAN, New England J. Med. **228**:533 (April 29) 1943.

The records of patients admitted to the Willard Parker Hospital for Contagious Diseases between Jan. 1, 1935 and April 1, 1941 were reviewed for the concomitant incidence of acute appendicitis.

Of 29,802 patients admitted to the hospital, 53 (0.18 per cent) showed gross and microscopic evidence of acute inflammation of the appendix. No patients with diphtheria had appendicitis, while 27 with measles had inflamed appendixes. Appendicitis occurred in 0.09 per cent of the patients with whooping cough and with scarlet fever, 0.12 per cent of the patients with rubella, 0.21 per cent of the patients with chickenpox, 0.27 per cent of the patients with measles and 0.47 per cent of the patients with mumps.

The records of 102 cases of acute appendicitis and pseudoappendicitis were analyzed for age, sex, leukocyte count and the time relation between the onset of appendicitis and manifestation of the contagious disease.

In more than half the cases of acute appendicitis the appendix was found to be already ruptured when the operation was performed.

Two patients with perforated appendix associated with measles and 2 with ruptured appendix associated with scarlet fever died.

A review of the literature is made, and some of the reported cases are included in the study.

GENGENBACH, Denver.

EXTENT OF IMMUNIZATION AND CASE HISTORIES FOR DIPHTHERIA, SMALLPOX, SCARLET FEVER AND TYPHOID FEVER IN 200,000 SURVEYED FAMILIES IN 28 LARGE CITIES. SELWYN D. COLLINS and CLARA COUNCELL, Pub. Health Rep. **58**:1121 (July 23) 1943.

At 8 years of age 61 per cent of the children in 200,000 surveyed families in twenty-eight large cities had been immunized against diphtheria, and 85 per cent had been vaccinated against smallpox. In no region was the rate of immunization against scarlet fever above 5 per cent. The number of immunizations against typhoid was negligible. Of preschool children the number that had been immunized against diphtheria and smallpox increased with the family income. Of children under 15 years of age the number of immuni-

zations against scarlet fever and typhoid increased with the family income, an evidence that immunizations are the result of individual initiative rather than of public programs.

SANFORD, Chicago.

• Acute Infectious Diseases

THE SIGNIFICANCE OF THE WIDAL REACTION IN ENTERIC DISEASES OF CHILDREN. MORRIS GREENBERG, *J. Pediat.* **23**:150 (Aug.) 1943.

The diagnosis of typhoid is frequently made on the basis of physical signs and symptoms and a positive reaction to the Widal test. However, even a high titer for typhoid agglutinins may be obtained in persons who have a *Salmonella* infection. The *Salmonellae* are closely related gram-negative, nonsporing, motile bacilli and include the organisms which cause typhoid, paratyphoid A and paratyphoid B as well as the so-called food poisoning organisms, such as *S. cholerae suis*, *S. typhi murium* and *S. enteritidis*. The *Salmonellae* are divided into a number of groups, each with a characteristic O antigen. The typhoid bacillus belongs in group D, together with several other species of *Salmonella*, such as *Salmonella enteritidis*, *Salmonella panama* and *Salmonella eastbourne*. An infection with any member of this group will cause the patient's serum to agglutinate the O antigen of this group, so that an infection caused by *Salmonella enteritidis*, for example, will cause agglutination of the O antigen of typhoid which is common to both. Similarly, an infection with *salmonella typhi murium* may give a high titer for the agglutination by the patient's serum of the antigen of paratyphoid B because *Salmonella typhi murium* and the paratyphoid B organism belong in the same group. In order to make a diagnosis of typhoid or paratyphoid, it is therefore important to examine the patient's stools for the causative organism, in addition to performing the other laboratory tests. Histories of several cases are given in which a preliminary diagnosis of typhoid or paratyphoid fever was made on the basis of clinical symptoms and a positive Widal reaction, while the ultimate diagnosis was infection with another species of *Salmonella*. A condensed table of the Kauffmann-White schema of classification is given, showing the grouping of the *Salmonellae* according to their antigenic structure.

SONTAG, Yellow Springs, Ohio.

TRICHINOSIS DURING CHILDHOOD. H. A. SLESINGER, *J. Pediat.* **23**:327 (Sept.) 1943.

During the past several years the incidence of trichinosis has been found to be much higher than previously considered. Slesinger reports a study of 18 cases of trichinosis occurring in children 2 to 15 years of age during the interval from November 1941 to February 1943. There was a small epidemic of this disease from October to December 1941. The youngest patient was 2 years old, 1 patient was 3 years old, and 5 were 8 years old.

The larvae, freed from their cysts in meat by the action of the gastric digestive juices, penetrate the intestinal mucosa, where the male and female sexual forms develop and mate within forty to seventy-two hours after the meat is eaten. The larvae are produced six to seven days after infection, and larval production may continue for six weeks or more. The larvae encyst chiefly in the voluntary muscles but may affect almost any organ of the body.

The symptoms in children are not as typical as in adults. In the cases reported the symptoms usually

consisted of fever (temperature 100 to 104 F.), headache, gastrointestinal upsets, muscular pains and occasionally edema of the eyelids or of the extremities. Only 4 patients had edema of the face and 2 edema of the lower extremities, of one to two days' duration. The number of eosinophils in the blood was relatively low. Some patients had no eosinophilia, and the highest count showed 32 per cent, in contrast to 80 per cent in adults. The eosinophilia was transient, and it appeared about one week after the onset of infection and subsided within a week. The number of white cells per cubic millimeter of blood varied from 7,050 to 36,900. The erythrocyte sedimentation rates were slightly to moderately increased. Of diagnostic value is the intradermal test, which consists of injecting 0.01 cc. of a 1:10,000 dilution of antigen prepared from powdered trichinal larvae. The test is read in fifteen to twenty minutes and a positive reaction consists of the development of a wheal surrounded by a zone of erythema; a delayed reaction may occur after thirty-six hours. The reaction to the test is not positive until the second week of infection. Eight of the 10 patients tested gave positive reactions. The precipitin test, which becomes positive on the tenth day after infection, was performed on all of the patients; 16 of the 18 had positive reactions. False, positive reactions occurred in a patient with typhoid fever and in another with undulant fever. Biopsy of muscle tissue would give the most conclusive evidence, but it is not practical.

Most of the patients were symptom free one week after admission to the hospital. One must differentiate trichinosis from influenza, acute nephritis, acute sinusitis and acute rheumatic fever. The treatment is symptomatic and consists of the administration of sodium salicylate or acetylsalicylic acid plus an opiate for relief of pain and the forcing of fluids; chemotherapy is of no value.

SHMIGELSKY, Chicago.

TYPHOID FEVER IN A SEVEN-MONTH-OLD INFANT. WALLACE SAKO and JOEL FLEET, *J. Pediat.* **23**:340 (Sept.) 1943.

A case of typhoid with recovery is reported in an infant 7 months of age. The literature indicates the rarity of the disease in infants and discloses the difficulties that may interfere with diagnosis of the condition.

The patient had a history and physical conditions typical of typhoid, although this is often not the case when typhoid fever occurs during infancy. Contaminated well water probably was the source of infection in this child. It is interesting to note that in this patient the Widal agglutination reaction did not become positive until the fever had subsided, approximately five weeks after the onset of the disease.

The current higher mortality from typhoid in infancy than in other age periods might be reduced if the disease were recognized promptly and the patient's fluid balance and nutrition adequately maintained.

SHMIGELSKY, Chicago.

CHRONIC MALARIA. R. A. GREENMAN, *M. Rec.* **155**:398 (Aug.) 1943.

A case of chronic recurrent malaria is reported with a comment on the difficulty of diagnosis and the frequent confusion with influenza and typhoid. The usual cause is the estivoautumnal parasite (*Plasmodium falciparum*). The disease has a gradual onset and may simulate many diseases. Chills may be a minor complaint. If laboratory identification of the parasite is

not successful the therapeutic test, with quinine, should be used; if the fever does not disappear with quinine, it is not malarial.

FERDINAND, Peoria, Ill.

ENDEMIC ROCKY MOUNTAIN SPOTTED FEVER IN MASSACHUSETTS. A. DANIEL RUBENSTEIN and HAROLD F. ROWLEY, *New England J. Med.* **229**:455 (Sept. 16) 1943.

All 5 of the infections observed in Massachusetts were acquired on Cape Cod.

The distribution according to the month of onset was as follows: May 1, June 1 and July 3. The dog tick, *Dermacentor variabilis*, which is the vector of this disease in the East, becomes most plentiful during the latter part of May or early in June and its prevalence declines sharply after mid July. There is usually a lag of several weeks between the time of maximum abundance of ticks and the peak in case incidence.

Two of the cases, those of a boy of 4 years and a girl of 8 years, are reported in detail.

GENGENBACH, Denver.

MALARIA IN INFANCY. HENRY A. REISMAN, *New York State J. Med.* **42**:1751 (Sept. 15) 1942.

Quartan malaria in a 3 month old infant was probably acquired from an intramuscular injection of the mother's blood soon after the child's birth. The baby recovered.

AIKMAN, Rochester, N. Y.

WAR-TIME DECLINE OF ACUTE RHEUMATISM. J. ALISON GLOVER, *Lancet* **2**:51 (July 10) 1943.

A decline in the incidence of rheumatic fever has been perceptible for many years. As early as 1930 Glover ventured to call it an "obsolescent" disease. Since the beginning of the war its gradual decline has greatly accelerated; the death rate has been halved. A general impression has been received of lessened incidence and decreased clinical severity of rheumatic fever, carditis and chorea.

The provision of supervisory centers and of hospital and convalescent accommodation for rheumatic children, important preventive measures as they are, can hardly have been developed enough before about 1930 to influence the decline appreciably.

The decrease in poverty caused by abundant employment during the war, the greatly increased provision of milk for all children and of solid meals for school children and the "long changes of air" due to evacuation, which has tended to decrease urbanization, are all possible factors in the sudden acceleration of decline.

But beyond and above all these factors Glover suggests that the main cause of the decline is a change in the relationship between man and the pyogenic streptococci. Is man becoming more immune, or, in other words, is *Streptococcus pyogenes* becoming less likely to provoke the rheumatic reaction, just as it seems to be becoming less toxigenic as measured by the incidence and severity of scarlet fever?

LANGMANN, New York.

BACILLARY DYSENTERY: CHEMOTHERAPY IN ITS TREATMENT. ERNEST BULMER and W. M. PRIEST, *Lancet* **2**:69 (July 17) 1943.

A series of 483 patients with nonamebic diarrhea, most of them with bacillary dysentery, were treated with sulfonamide drugs. Sulfaguanidine proved to be the most effective. Sulfanilamide and sulfapyridine were also used.

The stay in the hospital was substantially reduced for 323 patients treated with sulfaguanidine as compared with 600 controls.

LANGMANN, New York.

PERSISTENCE OF TETANUS ANTITOXIN IN MAN FOLLOWING ACTIVE IMMUNIZATION. D. G. EVANS, *Lancet* **2**:316 (Sept. 11) 1943.

Administration of a third dose of tetanus toxoid increases the concentration of antitoxin in the blood. For eighteen months at least the concentration remains much higher than that resulting from two doses of toxoid.

Two doses of tetanus toxoid, each of 1 cc., were given at an interval of nine weeks. The content of the circulating antitoxin in the serum was determined before and after the first injection and also four and ten months after the second. The effect of a third injection, given ten months after the second, was also investigated in 16 persons.

LANGMANN, New York.

THE SULPHAGUANIDINE TREATMENT OF SHIGA DYSENTERY IN NEW GUINEA. J. J. GARD, M. J. Australia **2**:188 (Sept. 4) 1943.

Gard reports uniformly good results in the treatment of 25 adults with bacillary dysentery with sulfaguanidine. An initial dose of 7 Gm. of the drug was followed by 3.5 Gm. every four hours for five doses daily. As soon as the number of stools was reduced to five or less a day the dosage was reduced to 3.5 Gm. three times daily and kept at that level until the stools remained normal for two or three days. The average number of days of treatment up to the time when the stools became normal in appearance and frequency was eleven and a half.

GONCE, Madison, Wis.

FASCIOLA HEPATICA IN A NINE MONTHS OLD CHILD. A. V. PAUSA, A. I. SANDOVAL, A. S. AZZI and M. G. VASQUEZ, *Arch. de med. inf.* **22**:163 (July-Sept.) 1943.

This is the first case of infection with *Fasciola hepatica* reported from Cuba. The source of infection was presumed to be berries or vegetables that contained the organism. The treatment used was the administration of 25 cg. of emetine hydrochloride in eighteen days by duodenal tube.

SANFORD, Chicago.

Chronic Infectious Diseases

THE USE OF ACETYLARSAN IN THE TREATMENT OF CONGENITAL SYPHILIS IN CHILDREN. JOSEPH YAMPOLSKY and CHARLES C. POWEL, *J. Pediat.* **23**:303 (Sept.) 1943.

Acetylarsan is a pentavalent compound containing 21.5 per cent arsenic. It occurs as a white powder freely soluble in water and is usually administered by subcutaneous or intramuscular injection although it may be given intravenously. The preparation, which is closely allied to and a derivative of acetarsone, is stated to be parahydroxyacetylaminophenylarsinate of diethylamine. Acetylarsan is supplied in an aqueous solution containing 23.6 per cent of the compound. This solution is neutral in reaction, colorless and clear and contains 5 cg. of arsenic per cubic centimeter; each cubic centimeter has an arsenic content equal to 0.25 Gm. of neoarsphenamine.

Dosage.—Acetylarsan is given intramuscularly, 0.5 cc. (0.025 Gm.) for each 20 pounds (9.1 Kg.) of body weight.

Course of Treatment.—Acetylarsan is supposed to be given in repeated courses of nine weeks of treatment alternated with six weeks of rest.

This drug seems to be well tolerated by children, and in the group of cases reported in this article only 1 child had diarrhea and a macular rash over the face, chest and arms with hyperpyrexia for nine days. The following reactions, however, have been reported in the literature: hyperpyrexia and malaise; vomiting some hours after an injection, also nausea and vertigo; toxic erythematous eruption; albuminuria; jaundice, and Herxheimer's reaction. The most frequent phenomenon complained of is headache. This condition, of course, would be difficult to detect in young infants.

In patients between the ages of 3 weeks and 1 year all lesions cleared up promptly after twenty to thirty injections. However, reversal of serologic reaction was noticed in only 4 of 11 cases. Roentgenographically, improvement was noticed in 3 and complete disappearance of osseous lesions in 2 cases out of 6. In the remaining case there was still a considerable degree of syphilitic involvement of the bones.

In children from 1 to 12 years of age secondary lesions did not improve; however, in 1 child iridocyclitis showed definite improvement after treatment. Serologically no change was noticed. In only 1 case was roentgen examination made and evidence of the disease remained after thirty-six treatments.

On the basis of the foregoing facts the following conclusions have been drawn: 1. Acetylarsan does not bring about toxic reactions in young children. 2. In order to reverse the Kahn reaction in young children treatment should be continued for at least a year. 3. Cutaneous lesions and other manifestations in young children can be healed by the use of this drug. 4. Roentgenologic improvement of osseous lesions is seen more often in young than in older children. 5. Apparently older children do not respond to this drug alone, and the authors suggest the use of bismuth along with it for the improvement of lesions of late and latent syphilis.

YAMPOLSKY, Atlanta, Ga.

TUBERCULOSIS AT A CHILDREN'S HOSPITAL. MARGARET E. HARKER, *Lancet* 2:387 (Sept. 25) 1943.

An analysis of the records of patients with tuberculous infection admitted to the Hospital for Sick Children, Great Ormond Street, during the first six months of 1942 bears out the report of the Medical Research Council that there has been an increase in tuberculosis in children under 5 years of age. In 1942 2.98 per cent of the total admissions, as compared with 2.11 per cent in 1938, were for tuberculous infections.

LANGMANN, New York.

Diseases of Blood, Heart and Blood Vessels and Spleen

THE OCCURRENCE OF A VASOCONSTRICTOR SUBSTANCE IN BLOOD DURING SHOCK INDUCED BY TRAUMA, HEMORRHAGE AND BURNS. IRVINE H. PAGE, *Am. J. Physiol.* 139:386 (July) 1943.

Shock was produced in dogs by placing tourniquets around the extremities, by stripping and exposing the intestines, by means of hemorrhage and by means of burns, and it was found that in association with the condition of shock a substance appears in the plasma which causes vasoconstriction in rabbits' ears perfused with either calcium-free Ringer solution or plasma.

The author states the belief that this substance does not originate in the kidneys or adrenal glands and the destruction of the spinal cord or renal denervation does not prevent its appearance. Furthermore, evidence obtained from application of a method depending on "fatiguing" the vascular musculature suggests that the vasoconstrictor action of plasma from burned, bled or shocked dogs may be due to the presence of an identical or similar substance. The original paper should be consulted concerning the details of the experiments which were conducted.

STROESSER, Minneapolis.

Diseases of Nose, Throat and Ear

NONSURGICAL ASPECTS OF TREATMENT OF ACUTE LARYNGOTRACHEOBRONCHITIS. HARRY L. BAUM *Ann. Otol., Rhin. & Laryng.* 52:608 (Sept.) 1943.

Acute laryngotracheobronchitis occurs most frequently in young children during the seasonal epidemic of infections of the respiratory tract. It is first characterized by laryngitis with moderate fever, dry cough, subglottic edema and partial laryngeal obstruction. As it progresses, tracheobronchial inflammation and edema develop, with exudation of thick, tenacious secretions. As laryngeal obstruction progresses, the cough lessens, sometimes disappearing entirely, the temperature drops, sometimes to subnormal, and "pale cyanosis" develops as a result of suboxia and cardiac and circulatory exhaustion from prolonged violent respiratory effort (respiratory shock). If the laryngeal respiratory difficulty is relieved by timely surgical intervention, symptoms improve and the temperature rises rapidly because of renewed oxygenation, but edema and exudate are still present in the trachea and bronchi. If this goes on to obstruction, death occurs from exhaustion, obstructive atelectasis, pneumonia or all three. If there is bronchoscopic removal of the secretions, there is again improvement, but the inflammatory edema persists, and bronchoscopy must be done repeatedly. In spite of this the patient may die. Toxemia seems to play a secondary role but is often a factor, especially in those cases which terminate in pneumonia. The mortality is extremely high, as shown by the reports quoted from numerous authorities.

Baum feels that nonsurgical treatment gives the most hope and discusses his method. He uses convalescent human serum, which may often be secured from some other member of the family from whom the child acquired the basic infection. From 50 to 200 cc., depending on the size of the patient, is given, preferably intravenously; however, it may be given subcutaneously or intramuscularly. This procedure may be repeated if desired. If this type of serum is not available, then pooled human influenzal convalescent serum should be used. If the latter cannot be secured, or if an adjunct is needed in severe cases, human antistreptococcal (scarlet fever) convalescent serum should be used.

Humidified oxygen is exceedingly valuable for relieving respiratory distress and gives the necessary respite while other measures are in preparation or taking effect.

Hypertonic human plasma may give prompt relief of the subglottic and tracheal edema. The plasma comes in the dry form, and instead of restoring it to its full volume one adds only one fourth of the normal volume of water, which gives a mixture containing four times the normal proportion of plasma protein. This mixture can be given intravenously with perfect safety. By osmotic action it withdraws the fluid from the edema-

ous tissues into the blood, relieving the obstruction. An initial dose of 25 to 40 cc. is usually sufficient; it may be repeated as often as necessary. If this is to be given, particularly after recent administration of conalescent serum or in the presence of suspected pulmonary stasis or evident circulatory embarrassment, venesection is advisable, with letting of blood to about four times the volume of the concentrated plasma to be administered.

Surgical intervention for the relief of dyspnea, especially tracheotomy, frequently has serious consequences, predisposes to difficulties in the lower respiratory tract and is to be avoided if prompt and adequate relief can be obtained without it. Surgical methods must, however, be resorted to without delay in certain cases when it is seen that nonsurgical treatment is not securing the desired results.

M. V. MILLER, Philadelphia. [Arch. OTOLARYNG.]

MEDIASTINAL EMPHYSEMA AND PNEUMOTHORAX FOLLOWING TRACHEOTOMY. GILBERT B. FORBES and G. W. SALMON, J. Pediat. 23:175 (Aug.) 1943.

Whenever tracheotomy is performed on a patient who exhibits severe respiratory obstruction or labored respiratory efforts, the possibility of the development of mediastinal emphysema must be considered. Four cases in which this occurred are presented. The symptoms are those of cyanosis and respiratory distress, and occasionally sudden death occurs. Mediastinal emphysema is easily diagnosed by fluoroscopy with the patient in the lateral position, and the pneumothorax which may result from the emphysema, by the usual signs. Simple aspiration of the air is often sufficient to relieve the symptoms which arise from the latter condition; it rarely succeeds in alleviating the emphysema because of pocketing of the air in the loose mediastinal tissues. Various possible mechanisms responsible for the emphysema are discussed; the most likely is the suction of air into the mediastinum along the fascial planes of the neck. Pneumothorax presumably occurs by the escape of air through a rupture in the relatively thin mediastinal pleura, aided by the decreased intrathoracic pressure resulting from inspiratory efforts against an obstructed airway. SONTAG, Yellow Springs, Ohio.

HEMOPHILUS INFLUENZAE TYPE B LARYNGITIS WITH BACTEREMIA. P. G. DUBOIS and C. ANDERSON ALDRICH, J. Pediat. 23:184 (Aug.) 1943.

Four cases of laryngitis and bacteremia caused by Haemophilus influenzae type B are reported. The clinical picture first described by Sinclair is emphasized because with it in mind the diagnosis may usually be made on inspection. The condition is characterized by (a) acute onset, (b) extreme prostration or "shock" out of proportion to the local symptoms, (c) severe laryngitis with extreme edema and hyperemia of both the false and true cords, (d) fever and (e) definite neutrophilic leukocytosis. The diagnosis is made accurately when H. influenzae is demonstrated in cultures of blood and of material from the larynx. Vigorous treatment with sulfonamide drugs after prompt tracheotomy was followed by early recovery in 3 of the 4 patients. The fourth patient recovered after a stormy, complicated course. Tracheotomy is advised because most of these patients are exhausted to the point of collapse, and the surgical procedure seems to decrease the severity of the disease and to shorten its course.

SONTAG, Yellow Springs, Ohio.

EMOTIONAL DISTURBANCES OF CONSTANT PATTERN FOLLOWING NONSPECIFIC RESPIRATORY INFECTIONS. HELEN G. RICHTER, J. Pediat. 23:315 (Sept.) 1943.

The observations reported in this study were made in the Department of Pediatrics, Yale University School of Medicine and the Children's Clinic, New Haven Hospital.

Since December 1940, 12 children have been observed and treated for diffuse emotional disturbances following mild infections of the upper respiratory tract. In each case a supposedly "normal" child had an illness diagnosed as "flu," "grippe," "tonsillitis" or "cold." In each instance the infectious phase was mild with low febrile response and the duration of this phase was short, ranging from a few days to one week. In all these cases a well defined change in personality was established within one month after the onset of the illness.

The analysis of the emotional disturbances revealed a syndrome of anxiety, depression and anancastic manifestation, that is, compulsive, obsessive phobic thinking and behavior. Also similar in these cases were the sequences in type and time relationships through which the symptoms developed and resolved themselves: (1) a short interval (one to two days) which was characterized by features similar to a quasidelirium, with motor restlessness, apprehension, tension and lability in mood; (2) a period of heightened anxieties and a depressive mood with an apparent onset of compulsions and obsessions, of varying duration. Subsequently these children withdrew from their everyday interests. At first the withdrawal was from the less familiar and the more recently acquired expressions of socialization; later, from the more superficial interpersonal relationships. Finally, contact with familiar persons was severely disturbed.

At the height of the emotional illness these children were preoccupied, at times "wooden," slightly retarded, sad, at times irritable, uncooperative, demanding, self accusatory, resentful, fearful, anxious and terrified. They were busy in the performance of rituals and repetitious acts meaningful to them. Sleep and the intake of food were frequently disturbed. School work was marked by failure.

Recovery was slow but also revealed certain patterns of progression. The first indications of change were usually improvements in mood and in motor activity. The stages of regression which followed were of varying duration. These regressive interests and activities were appropriate for chronologic levels lower by several years than the patients' actual ages and seemed to be proportionate to the severity of the entire emotional illness. A gradual subsidence of the gross compulsive and obsessive activities came relatively late in the recovery phase. In all cases, one of the last adjustments made was in the ability to cope with the school program, fulfilling both academic and social requirements. It would seem that the recovery phase reversed the process of withdrawal. The children felt increasingly secure enough to return to interests in enlarging fields of activity. Their interpersonal readjustments started in the family group and later extended to multiple contacts with various people.

Specific bacteriologic agents, vitamin deficiencies, drug intoxications or chronic illnesses could not be considered contributing etiologic factors.

A survey of the possible pertinent literature did not reveal descriptions of this type of symptomatic neurosis in association with mild infections of the upper respiratory tract.

Differential diagnosis must be made between sequelae of "influenza," psychotic states associated with epidemic influenza, emotional disturbances associated with chronic encephalitis, some forms of delirium, anxiety states, conditions allied to manic-depressive psychoses and the more classic "compulsive neurosis." Although there are certain similarities between the behavior observed in the present series and in any one of the clinical entities listed, not one of the latter is characterized by an initiating infection of the upper respiratory tract followed by quasilirium which ushers in compulsive behavior of varying duration.

The personality configurations of the children in whom this illness developed were strikingly similar: characterized by subservience, docility, perfectionistic striving and nonaggressive behavior. During the illness the children became overtly aggressive with associated strong feelings of guilt and with attempts to counteract these manifestations by compulsions and obsessions.

The prognosis is favorable. Spontaneous recovery may be expected in six to nine months.

Therapy must first be directed to supportive measures to treat the initiating infection. In the early stage of personality disturbance anxiety, restlessness and changes in mood are dominant; psychotherapy may be started in this period. Hospitalization for the more acute disturbances is advised chiefly to obtain adequate sedation (chemical and hydrotherapeutic), personal reassurance and protection from suicidal attempts and from too destructive, aggressive behavior. After the acute stage is passed prolonged psychotherapy is needed to bring to the child's understanding the psychologic mechanisms involved in his personality problems and thus to strengthen and hasten the spontaneous recovery.

RICHTER, New Haven, Conn.

A HEARING AID CLINIC. B. H. SENTURIA, S. R. SILVERMAN and C. E. HARRISON, *J. Speech Disorders* 8:215 (Sept.) 1943.

Seventy-five unselected cases of deafness are reported. Of these, 19 were instances of conduction deafness, 29 of mixed deafness and 17 of perception deafness. Thirteen hearing aids approved by the Council on Physical Therapy of the American Medical Association were tested for efficiency with various types of deafness; some are better than others, depending on the type of deafness. A slight increase in hearing may result in a great increase in intelligibility due to the fact that gaps in the auditory pattern are filled. The authors believe that a period of acoustic training is desirable after the acquisition of a hearing aid.

PALMER, Wichita, Kan.

AUDIOMETRIC TESTING AND HEARING CONSERVATION IN THE PUBLIC SCHOOLS. HORACE NEWHART, *J. Speech Disorders* 8:237 (Sept.) 1943.

State plans for the audiometric testing of children are essential. Every public school pupil should have a screening test and if necessary a later audiometric test by a physician.

PALMER, Wichita, Kan.

HEARING DEFICIENCIES AND SPEECH PROBLEMS. RAYMOND CARHART, *J. Speech Disorders* 8:247 (Sept.) 1943.

The author summarizes the literature dealing with the influence of loss of hearing on speech and reveals a number of inconsistencies. He suggests a series of problems which need much further investigation.

PALMER, Wichita, Kan.

LIP READING—A CONTINUING NECESSITY. HARRI MONTAGUE, *J. Speech Disorders* 8:257 (Sept.) 1943.

The values of lip reading and of modern schools for the teaching of lip reading are outlined.

PALMER, Wichita, Kan.

A CINEMATOGRAPHIC TECHNIQUE FOR TESTING VISUAL SPEECH COMPREHENSION. MARIE KATHERINE MASON, *J. Speech Disorders* 8:271 (Sept.) 1943.

Mason reports the changes made in the revision of her moving picture tests of ability in lip reading based on additional cases and showing a great increase in reliability. The test is given by silent film and is suitable for children aged 6 to 12 years.

PALMER, Wichita, Kan.

THE REALITY OF THE ZERO REFERENCE LINE FOR PURE TONE TESTING. HAROLD WESTLAKE, *J. Speech Disorders* 8:285 (Sept.) 1943.

A controlled study of 100 normal subjects makes it clear that the zero reference line of the audiometer, the theoretic threshold, is not completely objective. When subjects watch the dials of the 6A audiometer they come close to the zero reference line. When they do not watch the dials there is a considerable dispersion away from the zero reference line.

PALMER, Wichita, Kan.

THE EFFECTS OF NOISE AND CONCUSSION ON HEARING. H. B. PERLMAN, *J. Speech Disorders* 8:289 (Sept.) 1943.

The specific acoustic and physiologic factors that relate noise and concussion to the auditory sense are analyzed. Sensitivity to high frequencies is often lost through acoustic trauma. The author reports considerable personal clinical experience and reviews the literature. The results observed during the Spanish Civil War are cited to show various effects of sudden large pulses of sound. Cerumen in the ears may rupture the ear drum. Occasionally fracture of the temporal bone occurs. Many cases of deafness due to noise or concussion are not reported; a manual laborer, for example, will not be as aware of a loss in degree of hearing as keenly as a musician.

PALMER, Wichita, Kan.

THE DIAGNOSIS AND TREATMENT OF LUDWIG'S ANGINA. ASHBEL C. WILLIAMS and WALTER C. GURALNICK, *New England J. Med.* 228:443 (April 8) 1943.

The mortality in the present series was 10 per cent, compared with 54 per cent in an earlier one.

In the previous report the source of the infection appeared to be dental in 51 per cent of the cases. It was surprising to discover that a dental lesion was apparently the initiating factor in 18 (90 per cent) of the present series.

Streptococci have long been known to predominate as the causative organisms in Ludwig's angina. The presence of other organisms that grow best anaerobically has been mentioned previously.

The authors have been unable to control the disease in any instance by treatment with sulfonamide drugs alone.

It is recommended that the trachea be exposed or tracheotomy completed with local anesthesia. This having been done and an airway or a potential airway thus assured, pentothal sodium should be administered intravenously and the incision and drainage carried out with the patient anesthetized with the latter drug.

oxygen should be administered nasally during the second phase of the procedure.

GENGENBACH, Denver.

PINA BIFIDA AND CRANIUM BIFIDUM: IV. AN UNUSUAL NASOPHARYNGEAL ENCEPHALOCELE. FRANC D. INGRAHAM and DONALD D. MATSON, New England J. Med. **228**:815 (June 24) 1943.

The fourth paper in this interesting series is, like its predecessors, well illustrated. The diagnostic and surgical procedures for handling an encephalocele of a rare type are presented in detail.

GENGENBACH, Denver.

RADIUM TREATMENT OF GRANULAR OR HYPERTROPHIED LATERAL PHARYNGEAL TONSILLAR BANDS. ROBERT E. FRICKE and PETER N. PASTORE, Radiology **41**:256 (Sept.) 1943.

In chronic pharyngitis the lymph follicles covering the entire pharynx and nasopharynx are hypertrophied, and raised patches due to lymphoid cells around the ducts are easily seen. This condition is the so-called granular pharyngitis. When lateral pharyngeal tonsillar bands are hypertrophied, the infection is usually termed "lateral pharyngitis." Elimination of all infected tissue in Waldeyer's ring cannot be accomplished by operative procedures alone; only the faucial or palatine tonsils can be completely removed surgically. After the operation there is a tendency, in some instances, for the lateral pharyngeal bands or the tonsillar plaques in the lateral pharyngeal walls to undergo hypertrophy. Treatment by a variety of therapeutic measures has not been satisfactory. Although granular pharyngeal tonsillar bands are occasionally unattended by symptoms, they are a potential source of acute infection and of a painful and disabling sore throat.

Small doses of radium were safely employed, using an especially designed radium applicator, with gratifying success. A metal rod is threaded at the end so that a brass and silver tube containing radon can be attached; a hinged joint has been introduced just behind the attachment. The end of the rod, with the tube containing the radon attached, is passed through the nostril under topical anesthesia. When the rod is turned, the hinged portion drops downward and lies against the hypertrophied lateral band. The hinge is constructed to lock at an angle of about fifty degrees, the lateral pharyngeal wall.

so that the long axis of the radon tube presses against the band. The dose of radium used varied in the earlier cases from 1.5 to 4.5 gram minutes, but later it was standardized at 3 gram minutes to each lateral pharyngeal tonsillar band. Usually about 50 millicuries of radon was used; hence, one hour's application through each nostril furnished the planned dose. Twenty patients had only one treatment each with radium; 4 had two treatments each, a few months apart. Two of the 24 patients were given roentgen therapy, and 3 of them had surgical treatment in addition to the radium therapy. The authors consider it probable that the treatment will need repetition from time to time, because of the recovery of the lymphoid structures after several months.

ANSFACH, Chicago.

SYMPOSIUM ON SINUSITIS IN INFANCY. A. CODINACH, R. MACHADO and S. FUENTES, Arch. de med. inf. **22**:133 (July-Sept.) 1943.

The etiology of sinusitis was discussed by Dr. Ortega, the symptomatology by Dr. Cruz and the treatment by Dr. Codinach. This symposium should be read by those

interested in this field, as it cannot be successfully abstracted.

SANFORD, Chicago.

SUFFOCATING LARYNGITIS. S. GONZALEZ AGUIRRE, B. MESSINA and R. REY SUMAY, Rev. Soc. puericult. Buenos Aires **9**:242 (July-Sept.) 1943.

A review of the literature on suffocating laryngitis is presented.

The causation, pathogenesis and clinical picture of the condition are discussed. The authors state the belief that menthol present in "Vick's Vaporub" plays an important role in the production of laryngospasm by aggravating the general condition. Ten cases of suffocating laryngitis are presented; 5 patients died. The use of various therapeutic measures and medications, including intubation, tracheotomy, direct tracheobronchial aspiration through the endoscope, steam, sulfonamide and derivatives of it (administered locally and generally), antispasmodics (phenobarbital or aconite) and calcium gluconate (administered intravenously) is discussed.

The use of opium, which suppresses the cough reflex, or of belladonna, which dries up secretions, making difficult their expulsion, is contraindicated. In all 10 cases diphtheria toxoid-antitoxin was used.

BRIBIESCA, Mexico.

Diseases of Lungs, Pleura and Mediastinum

THE DIAGNOSIS OF VIRUS AND BACTERIAL PNEUMONIA IN CHILDREN. MAXWELL FINLAND, New England J. Med. **229**:201 (July 29) 1943.

In general, the recent tendency has been to make a diagnosis of virus pneumonia when a person fails to respond to treatment with a sulfonamide drug. However, one must remember two things: In the first place, even the common bacteria that are known to respond to the action of sulfonamide drugs are sometimes resistant; this is occasionally true of pneumococci; secondly, pneumonia due to organisms like streptococci and staphylococci requires prolonged and intensive treatment.

Of the nonbacterial agents causing pneumonia, the commonest is the virus of influenza, which is capable of producing various lesions in the lungs. It may also predispose the patient to severe bacterial infections, particularly with staphylococci or with influenza bacilli and sometimes with other organisms, such as streptococci.

GENGENBACH, Denver.

Diseases of the Gastrointestinal Tract; Liver and Peritoneum

BENEFICIAL EFFECT OF SMALLPOX VACCINE ON CURRENT APHTHOUS ULCERS OF MOUTH AND TONGUE. ARTHUR W. GRACE, Arch. Dermat. & Syph. **48**:151 (Aug.) 1943.

The author repeatedly inoculated 2 patients with aphthous ulcers of mouth and tongue with smallpox vaccine on the assumption that the condition is probably caused by a virus akin to that of herpes simplex, a disease which when recurrent is frequently controlled by such treatment. Both patients showed great improvement.

JACKSON, Iowa City.

CHEMICAL AND ENZYMIC STUDIES OF THE DUODENAL CONTENTS OF INFANTS. LASLO KAJDI and WILBURT C. DAVISON, J. Pediat. **23**:204 (Aug.) 1943.

The specific gravity of duodenal contents under fasting conditions (uncontaminated by gastric contents) was

low (1.002 to 1.010). The surface tension was fairly constant (31.6 to 35.3 dynes or 0.434 to 0.484 times that of distilled water). Variations in the p_H and in the amounts of bile acids and pancreatic enzymes present apparently were not related to changes in surface tension. Some factors responsible for this relatively constant surface tension were discussed, lecithin—cholesterol antagonisms, influence of proteins on the surface tension of bile salt solutions, changes in the p_H and the paradoxical effect of dilution. The p_H of duodenal contents under fasting conditions varied from 6.8 to 8.2 and the content of trypsin from 32 to 372 units per cubic centimeter and of amylase from 56 to 6165 units per cubic centimeter. There was no apparent relationship between the time elapsed since the last meal and the enzymic activity of the duodenal fluid. Secretion of trypsin and amylase was greatly reduced in patients with diarrhea. The rate of formation of duodenal fluid during fasting varied from 4 to 31 cc. per hour.

SONTAG, Yellow Springs, Ohio.

STUDIES OF NITROGEN AND FAT METABOLISM ON INFANTS AND CHILDREN WITH PANCREATIC FIBROSIS.

ALFRED T. SHOHL, CHARLES D. MAY and HARRY SHWACHMAN, J. Pediat. 23:267 (Sept.) 1943.

Infants and children with pancreatic fibrosis show a type of metabolism which closely approximates that described as occurring in dogs with blocked pancreatic ducts. It is characterized by the excretion of feces with a high dry weight and large content of nitrogen; the content of fat is moderately increased when the patient is fed a diet derived from casein hydrolysate, but since this contains no native protein, the dry weight of the feces, and the content of nitrogen and of fat were little affected. The addition of pancreatin to a diet containing both protein and fat was followed by some reduction in the total amount and nitrogen content of the feces but caused no change in the amount of fat excreted. The amount of fecal excretion and the nitrogen in the feces were reduced to within normal limits when a fat-free ration consisting of casein hydrolysate and dextrose was administered.

AUTHORS' SUMMARY.

OBSTRUCTION OF THE LARGE BOWEL IN NEWBORN INFANTS DUE TO CONGENITAL BANDS. JERRY ZASLOW, J. Pediat. 23:337 (Sept.) 1943.

It is the purpose of this paper to describe the clinical picture found when there is a simple obstruction of the large bowel in newborn infants. Although there have been infrequent reports of cases of obstruction of the colon, it appears that there are no proved cases of obstruction of the large bowel due to extrinsic bands in the absence of other malformations.

In infants obstruction of the large bowel produces a symptom complex like that occurring in adults with similar obstructions. There is marked abdominal distention, and vomiting, if present at all, is late in appearing. This is demonstrated by 2 cases recorded at Jewish Hospital in Philadelphia. In both cases distention appeared soon after birth and was progressive. Vomiting was a minor symptom, late in appearing, and was not severe until just before death. Stools were passed until just before death. There was little loss of weight. Postmortem examination in both cases revealed a peritoneal sheet extending from the under surface of the liver to the hepatic flexure of the colon. This band constricted the lumen of the bowel enough to produce a gradual accumulation of material proximal to the obstruction, although some fecal material was able to

pass. Since vomiting was not a prominent symptom enough food was ingested to reach the obstructed area and produce sufficient pressure to lead to necrosis of the proximal portion of the bowel.

"Abdominal distention out of proportion to the amount of vomiting, in spite of repeated bowel movements, should suggest to the physician the presence of an obstructing band around the large bowel." "The surgical procedure in early cases is obviously simple (cutting bands). If intervention is decided upon too late more radical operations will be necessary."

SHMIGELSKY, Chicago.

HIRSCHSPRUNG'S DISEASE. MARGARET HAWKSLEY, Proc. Roy. Soc. Med. 36:586 (Sept.) 1943.

Five cases of megacolon, selected from a series of 14 cases, are reported to demonstrate certain points in the differential diagnosis of Hirschsprung's disease and its treatment by spinal anesthesia. The technic of the spinal anesthesia is briefly described.

WILLIAMSON, New Orleans.

ANOREXIA IN INFANTS. M. BARACHUK, Rev. Soc. puericult. Buenos Aires 9:236 (July-Sept.) 1943.

Of 2,800 infants, newborn to 2 years old, examined in Buenos Aires, 381 were found to have anorexia. The causes of the anorexia were classified, and percentages were computed. The most common causes were infections of the respiratory tract (27 per cent), dystrophies (15 per cent) and irregularity in feeding, mostly due to prolonged breast feeding exclusively or inability to accept new flavors (23 per cent). In the rest of the infants, except 10 per cent with anorexia of unknown cause, the condition was due to causes such as other infections, stomatitis, teething, inappropriate surroundings, pruriginous dermatitis and congenital heart disease.

BIBIESCA, Mexico.

APPENDICITIS IN INFANTS. A. VIDAL FREYRE and A. CABALLERO, Rev. Soc. puericult. Buenos Aires 9:262 (July-Sept.) 1943.

The authors present a review of the Argentinian literature on appendicitis in infants under 2 years of age. Ten patients were seen and operated on, with a mortality of 10 per cent.

They state that appendicitis in infants if diagnosed and treated early has a good prognosis.

BIBIESCA, Mexico.

GASTRIC TETANY IN AN INFANT. C. M. PINTOS, VALENTIN O. VISILLAC and R. A. CELLE, Rev. Soc. puericult. Buenos Aires 9:270 (July-Sept.) 1943.

The authors present a case of tetany with pyloric tumor and gastric waves. The condition improved after a pyloromyotomy had been performed. Blood transfusions were given and fluids administered parenterally and intravenously, but the patient died from a secondary intestinal infection.

BIBIESCA, Mexico.

Nervous Diseases

TUBEROUS SCLEROSIS. ALEXANDER T. ROSS and WILFRED W. DICKERSON, Arch. Neurol. & Psychiat. 50:233 (Sept.) 1943.

This paper reports a detailed clinical study of 25 cases and a microscopic study of 3 cases of tuberous sclerosis. The authors consider the condition a developmental tissue dysplasia which is frequently familial.

Although most patients present idiocy, epilepsy and adenoma sebaceum, the variability of the clinical symptoms and the frequency of the condition are greater than is generally supposed.

BEVERLY, Chicago.

WHEAT GERM OIL (VITAMIN E) IN THE TREATMENT OF CONGENITAL NONOBSTRUCTIVE HYDROCEPHALUS. SIMON STONE, J. Pediat. 23:194 (Aug.) 1943.

Nine children with congenital nonobstructive hydrocephalus were treated with vitamin E in the form of wheat germ oil for periods ranging from three years to six months. The wheat germ oil was administered, in a mixture with vitamin B complex, in doses of 1 to 4 cc. of the oil daily. In all the patients treated arrest or evident slowing of the progressive hydrocephalus resulted. Improvement in visual acuity, reduction in the severity of nystagmoid movements of the eyes, increase in mental alertness and improvement in muscular tone and strength followed treatment. In the children with atrophy of the optic nerve who showed no response to visual stimuli before treatment was begun, reappearance of vision was demonstrated in that they reached out correctly for objects placed some distance from them.

A congenital disturbance of the hematoencephalic barrier as the cause of the hydrocephalus is suggested. Vitamin E apparently exerts a regulating effect on capillary permeability and thus aids in the adjustment of the mechanism for the secretion and absorption of spinal fluid. Whether a vitamin E deficiency in the pregnant mother was responsible for the development of the hydrocephalus and improvement therefore followed administration of the vitamin, or whether the improvement was due to the nonspecific effect of certain factors present in vitamin E on the cell membrane in the capillaries or on the blood constituents or was produced indirectly through action on the pituitary, is yet to be determined. The improvement in vision exhibited by these patients can be explained by the mechanical removal of excess fluid from the sheaths of the optic nerves. It is also probable that the myotropic and neurotropic factors contained in vitamin E played a part in producing the improvement in muscular strength and tone.

The salutary effect of vitamin E on the rate of absorption of exudates in such divergent conditions as multiple rheumatoid arthritis and rheumatoid myositis and in selected cases of muscular dystrophy, cretinism and hydrocephalus suggests one common denominator in these conditions, namely, excessive hydration of tissues caused by changes in cellular permeability, with vitamin E apparently as an efficient nonspecific regulator of this disturbance. The use of vitamin E in cases of nephrosis, nutritional edema and edema of unknown cause also deserves a therapeutic trial.

SONTAG, Yellow Springs, Ohio.

THE EFFECT OF REPEATED LUMBAR PUNCTURES ON THE SPINAL FLUID IN NORMAL CHILDREN. FRANK K. BAUER, New Orleans M. & S. J. 96:106 (Sept.) 1943.

The author performed two lumbar punctures within a period of forty-eight hours on each of 16 normal children. There was no increase in cell count at the second puncture. In the older children the pressure was slightly elevated at the second puncture and the values of the chemical constituents were slightly lowered.

BERKLEY, Los Angeles.

CONGENITAL CEREBRAL ANEURYSMS LATERALIZED BY ELECTROENCEPHALOGRAPHY. B. WOODHALL and H. LOWENBACH, South. M. J. 36:580 (Aug.) 1943.

The authors state that suggestive lateralization of the bleeding point in the affected hemisphere in "spontaneous" subarachnoid hemorrhage may be obtained by study of the electroencephalogram during the period of active hemorrhage. A more or less distinct asymmetry of amplitude, frequency and wave form between the tracings obtained from the two hemispheres is characteristic, with the abnormal record representing the hemisphere containing the bleeding point. This abnormal activity may be due to relative cerebral anoxemia, resulting from rupture of a congenital cerebral aneurysm, the common cause for such hemorrhages.

SCHLUTZ, Chicago.

Psychology and Psychiatry

ON THE ETIOLOGY AND THE PREVENTION OF MONGOLISM. CLEMENS E. BENDA, NEIL A. DAYTON and RUTH A. PROUTY, Am. J. Psychiat. 99:822 (May) 1943.

The authors summarize and analyze the theories regarding the causation of mongolism. The three main possible etiologic factors are (1) hereditary determination, (2) damage to the germ plasm (paternal or maternal) and (3) a noxious factor within the mother during gestation. Each of these factors is carefully discussed and evaluated from evidence in the literature as well as from the personal observations of the authors.

If mongolism were due to hereditary factors, they reason, the incidence of mongolism should increase in proportion to the number of offspring in accordance with mendelian expectation. Although many mongoloid children have five to twelve siblings, multiple incidence of mongolism is not found in the families. Research on twins refutes the theory of germinal damage.

The authors state the belief that mongolism is due primarily to a pathologic condition in the maternal endocrine system during pregnancy. A careful study of the records of children with mongolism, the authors state, reveals that the birth of a mongoloid child may be expected or even predicted under certain circumstances. The mothers of many children with mongolism are found physiologically (endocrinologically) unprepared for pregnancy. It is advisable, therefore, to subject pregnant women to thorough biochemical and endocrine studies during the antepartum period. Such an approach might not prevent this disorder, but it might serve to reduce the number of persons with mongolism.

Pediatricians and obstetricians should read this excellent paper in its original form.

JAHR, Omaha.

MEASUREMENT OF INTELLECTUAL FUNCTIONS IN THE ACUTE STAGE OF HEAD INJURY. JURGEN RUESCH and BURNES E. MOORE, Arch. Neurol. & Psychiat. 50:165 (Aug.) 1943.

The status of consciousness immediately after injury to the head was determined in 190 patients by subjecting them to a series of psychologic tests. Complete failure in all the tests, failure on the serial subtraction test alone and impaired performance on several tests represent three degrees of intellectual defect.

Patients with severe injuries to the head leading to intracranial hematoma, fracture of the skull and a bloody spinal fluid have a higher incidence of total

intellectual incapacity of varying duration than patients with short loss of consciousness only. Prolonged coma, delirium and confusion were much more frequent with the severe lesions and did not occur in patients with simple loss of consciousness.

Examination of 85 patients on three consecutive days by the "100 minus 7" test revealed that during this period accuracy of performance improves more than speed. Complete restitution, however, required a period of weeks.

BEVERLY, Chicago.

A PRELIMINARY SCALE FOR THE MEASUREMENT OF THE MENTALITY OF INFANTS. A. M. SHOTWELL and A. R. GILLILAND, *Child Development* **14**:167 (Sept.) 1943.

A preliminary scale for measuring the intelligence of babies during the first three months of life is described. Thirty-two tests, chosen for objectivity in giving and scoring and suitability as measures of adaptability, were administered weekly to 41 children, beginning, in most instances, at the age of 1 week and continuing, when possible, through the twelfth week. A brief description of the tests, with methods of giving and scoring, is included. After the results had been analyzed, the items, with some changes and additions, were arranged into batteries, one each for the ages of 4 weeks, 8 weeks and 12 weeks, and the tests were administered to 94 babies. The mean percentages of items passed in each battery constitute tentative norms. Corrected coefficients of correlation of 0.72 and 0.80 between the results from the batteries for infants 4 weeks and 8 weeks old given at the same time to 4 week old babies and between the results from the batteries for infants 8 weeks and 12 weeks old given at the same time to the 8 week old babies are reported as rough indexes of reliability. The correlation between both batteries given at 4 weeks and again at 8 weeks was 0.47. Evidence thus far collected suggests that it will be possible to construct a valid and reliable measure of the intelligence of infants during the first three months of life, when the rate of mental growth is comparatively most rapid. Items to be retained ultimately are those showing (1) progression with age, (2) variability at any one age, (3) agreement with the total score and (4) correlation with intelligence quotients obtained at later ages.

PALMER, Washington, D. C.

Diseases of the Ductless Glands; Endocrinology

NATURE OF THE PITUITARY FACTOR STIMULATING MAMMARY DUCT GROWTH. J. J. TRENTIN, A. A. LEWIS, A. J. BERGMAN and C. W. TURNER, *Endocrinology* **33**:67 (Aug.) 1943.

That the pituitary hormonal complex contains some factor or factors involved in mammary growth is generally accepted. The present paper deals with the chemical nature (i. e., protein or lipid) of the pituitary factor responsible for the stimulation of growth of the mammary duct in the male mouse. When improved extraction procedures were used, the bulk of the activity of the fresh pituitary substance was recovered in the protein fraction rather than in the lipid fraction.

JACOBSEN, Buffalo.

EVIDENCE OF HYPOTHALAMIC CONTROL OF HYPOPHYSAL GONADOTROPIC FUNCTIONS IN THE FEMALE GUINEA PIG. F. L. DEY, *Endocrinology* **33**:75 (Aug.) 1943.

By observing the effects of lesions produced in the hypophysis and in the hypothalamus, it is concluded

that the hypothalamus and the median eminence may be concerned in the regulation of pituitary gonadotropic functions. It seems unlikely that they exert this control by nerve fibers that pass by way of the hypophysial stalk.

JACOBSEN, Buffalo.

EFFECTS OF THYROTROPIC HORMONE, GONADOTROPIC FACTOR, PITUITARY GROWTH SUBSTANCE AND INSULIN UPON THE PHOSPHATASE CONTENT OF RAT FEMURS. C. H. WEICHER and E. M. WATSON, *Endocrinology* **33**:83 (Aug.) 1943.

It has been shown that the administration of various glandular preparations, such as progesterone, testosterone, estradiol, thymus extract and thyroxine, is followed by an increase in the phosphatase content of the femur.

Further experiments, here reported, showed that both anterior pituitary extracts rich in the thyrotropic hormone and extracts rich in the gonadotropic factor, injected subcutaneously, caused an increase in the phosphatase content of both the diaphysis and the epiphyses.

The preparations of the growth-promoting factor of the anterior pituitary which were used did not exert a consistent influence on the bone phosphatase.

JACOBSEN, Buffalo.

GROWTH AND METABOLISM OF YOUNG HYPOPHYSECTOMIZED RATS FED BY STOMACH TUBE. LEO T. SAMUELS, ROGER M. REINECKE and KENNETH L. BAUMAN, *Endocrinology* **33**:87 (Aug.) 1943.

Young rats were hypophysectomized and then maintained by feeding through a stomach tube, on a food intake which caused growth in litter mates used as controls.

Although intestinal absorption was good the hypophysectomized rats showed an abnormally slow increase in skeletal growth, 10 per cent of that in the controls; and a small increase in nitrogen storage, about 30 per cent of that in the controls.

JACOBSEN, Buffalo.

ANTAGONISM OF PITUITARY ADRENOCORTICOTROPIC HORMONE TO GROWTH HORMONE IN HYPOPHYSECTOMIZED RATS. WALTER MARX, MIRIAM E. SIMPSON, CHOH HAB LI and HERBERT M. EVANS, *Endocrinology* **33**:102 (Aug.) 1943.

It has been observed that pituitary extracts rich in the adrenocorticotrophic hormone inhibited somatic growth in young castrated rats. The present communication reports the effect of extracts containing the adrenocorticotrophic hormone on the action of the growth factor, in the absence of the pituitary.

These experiments indicate that the antagonism between adrenocorticotrophic and growth hormones occurs in the absence of the pituitary gland. It cannot be attributed to a reduction in the food consumption. It would appear to result from opposing metabolic effects of these two factors.

JACOBSEN, Buffalo.

INCREASED SODIUM CHLORIDE AND WATER INTAKE OF NORMAL RATS TREATED WITH DESOXYCORTICOSTERONE ACETATE. KATHERINE K. RICE and CURT P. RICHTER, *Endocrinology* **33**:106 (Aug.) 1943.

The results of these experiments suggest that the primary effect of the administration of desoxycorticosterone in normal rats is an increased requirement of salt, resulting in an increased appetite for salt.

It is further suggested that the polydipsia of animals treated with desoxycorticosterone acetate on a high salt

ntake is a direct consequence of the latter rather than a manifestation of a primary effect on water metabolism.

JACOBSEN, Buffalo.

EFFECT OF THYROIDECTOMY ON RESISTANCE TO LOW ENVIRONMENTAL TEMPERATURE. C. P. LEBLONE and J. GROSS, *Endocrinology* **33**:155 (Sept.) 1943.

The role of the thyroid hormone in the resistance to cold is confirmed by the observation that adult rats thyroparathyroidectomized two weeks, previously died within a week at 0 to 2 C. while normal, parathyroidectomized and thyroxin treated thyroidectomized rats survived for several weeks at the same temperature.

Since the thyroidectomized rats lived in the cold for one or several days in good condition and then became moribund and died, it would appear that the high level of metabolism necessary for resisting cold could be reached but not maintained for more than a few days in thyroidectomized animals.

JACOBSEN, Buffalo.

STUDIES ON THE RESPONSE OF HYPOPHYSECTOMIZED RATS TO INTRAPERITONEAL GLUCOSE INJECTIONS. SAMUEL JOSEPH, MALVINA SCHWEIZER and ROBERT GAUNT, *Endocrinology* **33**:161 (Sept.) 1943.

Severe disturbances in the distribution of electrolytes and water in the body can be induced by the injection of solutions of dextrose intraperitoneally.

Death in both hypophysectomized and adrenalectomized animals following injections of dextrose is attributed to circulatory failure or shock. The classic symptoms of shock observed were fall in blood pressure, hemoconcentration, failure of peripheral circulation and reduced body temperature. These features of the syndrome developed in essentially similar fashion in both hypophysectomized and adrenalectomized animals, although perhaps somewhat more rapidly in the latter. This set of symptoms, indeed, was the clearly significant differential between normal and hypophysectomized rats.

Since these symptoms were relieved by administration of adrenal cortical extract, it is concluded that the deficiencies in the hypophysectomized animals were due to atrophy and hypofunction of the adrenal cortices.

From a variety of experiments it is apparent that adrenal cortical hormone is essential for the prevention of circulatory failure following stress. These experiments afford another example of susceptibility to circulatory failure in the absence of normal adrenal cortical function, in this case the primary deficiency being that of the pituitary adrenotropic hormone.

JACOBSEN, Buffalo.

EFFECT OF CONTINUED ORAL ADMINISTRATION OF DIETHYLSTILBESTROL ON BLOOD PRESSURE, HEART RATE AND RESPIRATION OF ALBINO RATS. CHARLES S. MATTHEWS, FREDERICK E. EMERY and PAUL L. WEYGANT, *Endocrinology* **33**:177 (Sept.) 1943.

Elsewhere there has been published evidence which indicated that diethylstilbestrol is capable of producing hypertension in rats. In the experiments reported here 45 adult oophorectomized rats and 35 normal male rats received by stomach tube 1 mg. of diethylstilbestrol in alkaline aqueous medium daily for periods up to one

hundred days. The results indicate no deviation from the normal range of values for the blood pressure.

JACOBSEN, Buffalo.

THE INTERRELATIONS OF SERUM LIPIDS IN PATIENTS WITH THYROID DISEASE. JOHN P. PETERS and EVELYN B. MAN, *J. Clin. Investigation* **22**:715 (Sept.) 1943.

Although the level of cholesterol in the serum rises when the thyroid gland is removed and falls when active thyroid preparations are given, normal concentrations of cholesterol may be found in the serum of patients with hyperthyroidism or with thyroid deficiency, because the level to which cholesterol falls or rises with these disorders is roughly related to the normal concentration of cholesterol of the affected subject.

The ratios of free to total cholesterol and of cholesterol to lipid phosphorus are not affected by disorders of thyroid function. The latter ratio, within the normal range of cholesterol, is the same for patients with normal, excessive or deficient thyroid activity, varying with the concentration of cholesterol. As the concentration of cholesterol falls below this range in hyperthyroidism the ratio diminishes as it does in malnutrition; as the concentration of cholesterol rises above this range the ratio rises to describe a continuous curve.

There is no relation between the level of cholesterol and the level of neutral fat in the serum.

[FROM THE AUTHORS' SUMMARY.]

MACROSOMIA, CARDIAC HYPERTROPHY, ERYTHROBLASTOSIS AND HYPERPLASIA OF THE ISLANDS OF LANGERHANS IN INFANTS BORN TO DIABETIC MOTHERS. HERBERT C. MILLER and HUGH M. WILSON, *J. Pediat.* **23**:251 (Sept.) 1943.

Roentgen examinations of the hearts of 10 infants born to mothers with diabetes mellitus showed that during the first ten days of life there is a significant increase in the size of this organ. Follow-up roentgenograms of these infants revealed that the size of the heart had assumed normal proportions by the end of the sixth week of life in almost all the cases. Post-mortem examination of the hearts of 18 infants born to mothers with diabetes demonstrated that in about half the infants the weight of the heart was abnormally increased, sometimes to as much as two or three times the expected weight. An abnormally heavy heart occurred more usually in an infant who weighed over 4,000 Gm. at birth. In addition to the cardiac changes there was an increase in the amount of erythropoietic tissue in the liver in about half of the infants examined at autopsy. In 3 of the 18 postmortem examinations macrosomia, cardiac hypertrophy, hyperplasia of the islands of Langerhans and excessive erythropoiesis in the liver were observed. These somatic and visceral changes occurred in some infants whose mothers were not diabetic either before or at the time the infants were born but who, subsequent to the delivery, became diabetic. The authors also observed these same changes in body weight and alterations in the heart, liver and pancreas in infants with erythroblastosis fetalis. The relationship between the cardiac hypertrophy and the symptoms in infants born to diabetic mothers is discussed. Also the possible relationship between diabetes mellitus and erythroblastosis fetalis is considered.

SONTAG, Yellow Springs, Ohio.

Book Reviews

A Hundred Years of Medicine. By D. C. Haagen-
sen and E. B. Lloyd. Price, \$3.75. Pp. 444, with
42 illustrations. New York: Sheridan House, Inc.,
1943.

This book was written with the hope, to quote from the preface of the English edition, "that it may prove of value not only to the layman, for whom it is primarily intended, but also to those medical practitioners and students who have not found time for my specialized study of the history of medicine." Here is a medical book for which one can earnestly hope the widest possible circulation. It cannot be endorsed too highly; so far as this reviewer knows, it is in a class by itself. It meets a need that is real and that other publications by medical columnists and by lay and professional writers for the laity do not meet. Its purpose is not to discuss isolated medical subjects but to tell the intelligent layman and the alert physician and student just what modern scientific medicine is and how it developed during the last hundred years. It is a fascinating story, well told. If every layman read this book there would be a better understanding of the things physicians are trying to do and the reasons for their attitudes toward the various aberrant practitioners and cultists. Of course the cultural value of such knowledge is unquestionable.

The book is written in a clear, simple style so that the layman need not be apprehensive about getting beyond his depth. Chemical terms are avoided as far as possible unless their meanings are evident from the context, and explanations are offered when necessary. The medical reader will not find that this in any way detracts from the historic and scientific accuracy or from the readability. There are probably few physicians who will not find many interesting and instructive facts that they have never known or have forgotten. Especially interesting are the brief biographic data on some of the great men and women who have helped to make modern medicine what it is.

There are forty-four well chosen and well produced illustrations and a comprehensive bibliography.

The book was first written by Dr. Lloyd, an English "specialist in public health." The American edition retains about one third of the English edition, with slight modifications to fit the American scene; the remainder of the book has been entirely rewritten by Dr. Haagen-
sen, a surgeon and pathologist on the faculty of the Columbia University School of Medicine.

The book is divided into four parts. Part I contains about sixty pages and is an introductory review of the development of medicine, surgery and hygiene up to the nineteenth century. Part II, of about 160 pages, deals with medical science during the last hundred years, under the following topics: pathology, diagnosis, the germ theory, chemotherapy, tuberculosis, the vitamins, pernicious anemia, diabetes, nephritis and diseases of the heart and lungs. In part III, about 140 pages, the authors discuss the advances in surgery during the last one hundred years, taking up anesthesia, surgical infection, control of hemorrhage and shock, obstetrics and gynecology, genitourinary surgery, orthopedics, neurosurgery, thoracic surgery, ophthalmology, otology, rhinology and laryngology, the use of radium and the

training of surgical nurses. Part IV, about 80 pages deals with the importance of social service and of infant welfare, including their effects on longevity and the medical and economic situation brought about by the greatly increased number of older people. Under "The Doctors' Dilemma," medical education, specialization the high cost of medical care, medical insurance, social medicine and group practice are considered.

A book of this kind is necessarily limited in its scope, but it does seem strange, and a matter of regret, that the marvelous development of pediatrics is wholly ignored. It is to be hoped that there will be many new editions and that in them this will be given due attention.

Clinical Diagnosis by Laboratory Examinations.
By John A. Kolmer. Price, \$8. Pp. 1,239, with
illustrations. New York: D. Appleton, Century Co.,
Inc., 1943.

This book, which is not a new edition of Kolmer and Boerners' "Approved Laboratory Technic," has been assembled entirely by Dr. Kolmer and is intended primarily for teaching in medical schools, as well as for the use of physicians and pathologists who need to correlate the clinical interpretations of laboratory examinations and to evaluate their practical applications in the diagnosis of disease.

Of the three parts of the book, the first, of 642 pages, is concerned with the clinical interpretation of laboratory examinations. It includes many useful charts summarizing abnormal results and observations and their various causes and giving normal values with their physiologic bases. This inclusive survey embraces the fields of hematology, physiologic chemistry, toxicology, bacteriology, immunology, parasitology, mycology, serology, allergy, endocrinology and vitamins and biopsy.

The second part, of some 330 pages, deals with the practical applications of laboratory examinations in clinical diagnosis, classifying the diseases of various organs and systems, interpreting the laboratory diagnoses and indicating the tests of value. Excellent summaries of the diagnoses of the arthritides, brucellosis, the steatorrheas and the venereal diseases are among these chapters. Some material found in the first part of the book is repeated.

The last, and smallest, section is concerned with technic; usually but one accepted method of laboratory procedure is given.

Necessarily in such a comprehensive book there are subjects treated rather summarily, such as parasitology, virus diseases and endocrinology. While numerous colored plates are devoted to cutaneous reactions, there is a lack of good illustrations in the section on hematology. There are an excellent index and an adequate bibliography.

This ambitious book will no doubt stimulate some adverse criticism, the well informed physician contending that it is sketchy and not always accurate, and the laboratory technician that there are few methods and those few described too briefly. However, as a source of reference for the average diagnostician, laboratory worker or teacher it will be appreciated by many.

The Year Book of Industrial and Orthopedic Surgery, 1943. Edited by Charles F. Painter, M.D. Price, \$3. Pp. 440, with 306 illustrations. Chicago: The Year Book Publishers, Inc., 1943.

This edition of the Year Book of Industrial and Orthopedic Surgery is made up of pertinent reviews of time-saving value. Material of interest to pediatricians and general practitioners as well as to orthopedic and industrial surgeons is included. Numerous contributions from the military and naval services should prove valuable to civilian practitioners and to surgeons in the armed forces. Since the supply of medical literature from European and Asiatic countries now engaged in war has been almost totally cut off, the sources of subject matter are primarily North and South America. A number of reviews from British journals are presented.

The major portion of the book covers orthopedic surgery, while the second part deals with industrial medicine and surgery. The orthopedic subject matter is arranged under such headings as fractures and traumatic dislocations, arthritis, tuberculosis, osteomyelitis, inflammatory conditions and poliomyelitis. The industrial material includes problems of organization and the war, absenteeism, fatigue, respiratory and cardiac conditions and specific hazards.

Of particular interest are articles dealing with internal and external fixation of fractures, the repair of bone in the presence of foreign fixation materials, therapy for arthritis, especially studies on the use of activated ergosterol (ertron), vitamins, gold salts and bee venom, the conservative treatment of acute osteomyelitis, ossifying lesions about tendons and bursae, the Kenny treatment of poliomyelitis, lesions of the intervertebral disks, pathologic conditions of the feet and operative technic. Numerous problems in industry, of current and future interest, are discussed.

These well selected reviews present the practical essentials of a large mass of literature. Individual articles are well written, brief and yet complete. The 1943 year book is a means whereby the harrassed practitioner can keep abreast of significant advances in industrial and orthopedic surgery, in spite of demands made on him by the war.

Child Development: Physical and Psychological Growth Through the School Years. By Marian E. Breckenridge, M.S., and E. Lee Vincent, Ph.D. Price, \$3.25. Pp. 592, with 37 illustrations. Philadelphia: W. B. Saunders Company, 1943.

This excellent presentation has been designed to bring together the current knowledge and philosophies relating to the pattern of total, or "organismic," growth of the infant and child. Emphasis is placed on the factors conducive to optimum response. The material is written in simple yet effective style. The volume should prove of value for every student of childhood, whether he is a physician, teacher, hygienist, welfare worker or parent. The authors not only portray the manner of organismic growth but show how its processes may be affected favorably or unfavorably by specific factors in the environment. The careful reader will gain insight into the superficial aspects of nutrition and child psychology; the scope of the material covered makes it impossible to offer the detailed specific information the advanced student in these subjects would desire. As a guide toward attainment of favorable nutritional and mental hygiene, however, the scope of the book is adequate.

The volume is divided into fifteen chapters. Each chapter is concluded by series of questions and of generic references to the literature, designed to aid the more detailed study of the material presented. The chapters are subdivided as to content, with convenient subtitles. From the viewpoint of the mature student, it would be useful if chapter summaries were provided as well. Records of illustrative cases are interspersed frequently. The material is well indexed, and the terminal bibliography is extensive and up-to-date.

Every physician whose activities bring him into association with children needs the insight which this book provides. The volume can be used either as a source of general information or for reference on the effects of specific environmental conditions.

Care and Feeding of Children. By L. Emmett Holt Jr., M.D. Sixteenth edition. Price, \$2. Pp. 321, with 2 illustrations. New York: D. Appleton-Century Company, Inc., 1943.

This is the sixteenth edition of a book for mothers written by L. Emmett Holt, M.D., in 1894 and revised and enlarged by his son, L. Emmett Holt Jr., M.D.

The book is fairly broad in scope, covering the care, growth and feeding (natural and artificial) of children. There are sections on the care of feeble and premature children and older children, the handling of behavior problems and the prevention and treatment of the common ailments of children.

The book is written in question and answer style, which seems to break the continuity of thought. However, the answers are simple, concise and scientifically correct. The style is especially effective in the section on behavior problems as it answers the questions that arise in almost every family.

The scope of this book is broad enough to include answers to most mothers' questions in regard to the day by day life of the child, but it does not intrude too far into the domain of the physician. It is truly a complete reference library for mothers.

The section on infant feeding is probably more elaborate than necessary for the layman. It describes too many varied types of feeding.

The part on behavior problems seems to be especially well written. It is scientific and suggests solutions to the problems about which mothers are so frequently puzzled such as the best way to handle certain difficult situations. The terminology is pleasingly simple and does not attempt to make pseudopsychiatrists of the mothers.

This volume is a good book of its type, and it can be recommended when such a book is requested.

The Health of Children in Occupied Europe. Edited by The International Labour Organisation. Price, 25 cents. Pp. 37, not illustrated. Montreal, Canada: La Patrie Publishing Company Limited, 1943.

This small pamphlet contains a tremendous amount of information, all of which is of interest to the average physician in the United States, for the situation among children in Europe is beyond his comprehension. The pamphlet deals mainly with the causes of the deficiencies in the diets. These are only part of the picture; the living conditions, the spread of disease and all the worst aspects and consequences of war are pictured in these pages. The facts raise the question as to how the amount of food necessary to rectify these conditions after the war can be supplied and transported.

Directory of Pediatric Societies *

INTERNATIONAL

INTERNATIONAL ASSOCIATION OF PREVENTIVE PEDIATRICS

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

INTERNATIONAL CONGRESS OF PEDIATRICS

President: Dr. Henry F. Helmholtz, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Charles F. McKhann, University Hospital, Ann Arbor, Mich.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston. Time: Postponed indefinitely.

INTERNATIONAL CONGRESS FOR THE PROTECTION OF INFANCY

Secretary: Prof. G. B. Allaria, Corso Eramante 29, Torino 120, Italy.

FOREIGN

ARGENTINE PEDIATRIC SOCIETY OF BUENOS AIRES

President: Dr. Martin Ramón Arana, 1809 Rodríguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguía, Cerrito 1179, Buenos Aires.

ASSOCIAÇÃO PAULISTA DE MEDICINA, SECTION ON PEDIATRICS

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Paulo de Barros Franca, Av. Brigadeiro Luiz Antonio 393, 1º Andar, São Paulo, Brazil.

BRITISH PAEDIATRIC ASSOCIATION

President: Prof. L. G. Parsons, 58 Calthorpe Rd., Five Ways, Birmingham.
Secretary: Dr. Donald Paterson, 27 Devonshire Pl., London, W. 1.

DANISH PEDIATRIC SOCIETY

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

NEDERLANDISCHE VEREENIGING VOOR KINDER-GENEESKUNDE

President: Dr. J. H. G. Carstens, Servaasbolwerk 14^a, Utrecht.
Secretary: Dr. R. P. van de Kastele, Leen van Poot 340, 's Gravenhage.
Place: Different places. Time: Three times a year.

PAEDIATRICKÝ SPOLOK NA SLOVENSKU

President: Dr. A. J. C. Churá, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Dr. E. A. Cockayne, 98 Harley St., London W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialkstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Angel A. Aballí Arellano, 17 No. 609 Vedado, Habana.
Secretary: Dr. Julio G. Cabrera Calderin, Hospital Mercedes L y 21 (Vedado), Box 2430, Habana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Fernando López Clares, 12/a. Medellín 191, Mexico.
Secretary: Dr. Jesus Gómez Pagola, Versalles 64, Mexico.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. E. Santos Mendoza.
Secretary: Dr. P. Oropeza, Hospital de Niños, Caracas.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Jose Alberto Praderi, Eduardo Acevedo 1132, Montevideo.
Secretary: Dr. Alfredo Ramon Guerra, Paysandú 824, Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Franklin P. Gengenbach, 1850 Gilpin St., Denver, Colo.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S
HOSPITAL SECTION

Chairman: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly, Mass.

AMERICAN PEDIATRIC SOCIETY

President: Dr. James L. Gamble, 300 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES
OF CHILDREN

President: Dr. R. R. Struthers, 906 Drummond Medical Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Joseph A. Johnston, Henry Ford Hospital, Detroit.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Eugene Smith, 385-24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Warren R. Sisson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. C. G. Ashley, 833 S. W. 11th Ave., Portland, Ore.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. Arild E. Hansen, University of Minnesota, Minneapolis.
Secretary-Treasurer: Dr. Albert V. Stoesser, 205 W. University Hospital, Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver.

SOUTHERN MEDICAL ASSOCIATION, SECTION
OF PEDIATRICS

Chairman: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.
Secretary: Dr. Angus McBryde, 604 W. Chapel Hill St., Durham, N. C.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Amas Gipson, 948 Forrest Ave., Gadsden.
Secretary-Treasurer: Dr. Ruth Berrey, 2021-6th Ave. N., Birmingham.

ARIZONA PEDIATRIC SOCIETY

President: Dr. Vivian Tappan, San Clemente, Tucson.
Secretary: Dr. Hilda Kroeger, Arizona State Health Dept. (Maternal and Child Welfare Division), Phoenix.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION
ON PEDIATRICS

Chairman: Dr. William C. Deamer, University of California Hospital, San Francisco.
Secretary: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Ludo Von Meysenbug, Box 3356, Daytona Beach.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. T. F. Davenport, 104 Ponce de Leon Ave. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB
OF CONNECTICUT

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Time: Three meetings a year.

ILLINOIS STATE MEDICAL SOCIETY, SECTION
ON PEDIATRICS

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Mark L. Floyd, Children's Hospital, Iowa City.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION
ON PEDIATRICS

Chairman: Dr. A. Clement Silverman, 508 E. Genesee St., Syracuse.
Secretary: Dr. Albert G. Davis, 307 Gas and Electric Bldg., Utica.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA,
PEDIATRIC SECTION

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucciesi, Philadelphia Hospital, Philadelphia.

MICHIGAN STATE MEDICAL SOCIETY,
PEDIATRIC SECTION

Chairman: Dr. Charles F. McKhann, University Hospital, Ann Arbor.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. E. W. Hancock, 820 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. John M. Thomas, 1102 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Arthur H. London, 1105 W. Main St., Durham.
Secretary: Dr. Jay M. Arena, 604 W. Chapel Hill St., Durham.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Ben H. Nicholson, 301 N. W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Lonita Bogg, 301 E. Coffee St., Greenville.
Secretary-Treasurer: Dr. Hella Sheriff, Wade Hampton Office Bldg., Columbia.

TEXAS PEDIATRIC SOCIETY

President: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Edwin A. Harper, 301 Rivermont Ave., Lynchburg.
Secretary: Dr. Emily Gardner, 1100 W. Franklin St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY,
SECTION ON PEDIATRICS

President: Dr. Andrew Amick, 1021 Quarrier St Charleston.
Secretary: Dr. A. A. Shawkey, Professional Bldg Charleston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND
PEDIATRIC SECTION

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave Cleveland.
Secretary: Dr. I. B. Silber, 10465 Carnegie Ave Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO,
SECTION OF PEDIATRICS

President: Dr. I. Nelles Silverthorne, 170 St. George St., Toronto, Canada.
Secretary: Dr. G. P. Hamblin, 2333 Bloor St. W Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry J. Cohen, 1975 Walton Ave New York.
Secretary: Dr. Walter Levy, 12 E. 88th St., New York
Place: Concourse Plaza Hotel, 161st St., and Grand Concourse. Time: Second Wednesday of each month except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Harry A. Naumer, 37-8th Ave Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St Brooklyn.
Place: Granada Hotel. Time: Fourth Wednesday of October, November, February, March and April.

BUFFALO PEDIATRIC SOCIETY

President: Dr. A. Wilmot Jacobsen, 187 Bryant St Buffalo N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave Buffalo, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Edward J. Wynkoop, 501 James St Syracuse.
Secretary: Dr. Frank J. Williams, 58 S. Swan St Albany.
Places: Various cities in New York. Time: Third Tuesday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Morley D. McNeal, 2 N. Sheridan Rd Highland Park, Ill.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

CINCINNATI PEDIATRIC SOCIETY

Secretary: Dr. T. Selkirk, 3530 Reading Rd., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati.
Time: On call.

President: Dr. Lloyd K. Felter, 3144 Jefferson Ave., Cincinnati.

DALLAS PEDIATRIC SOCIETY

President: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas, Texas.

Secretary-Treasurer: Dr. Gladys J. Fashena, 4585 Bel-
fort, Dallas, Texas.

Place: Bradford Baby Hospital. Time: 1 p. m., second
and fourth Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. Hugh Lewis, Detroit, Mich.

Secretary: Dr. John J. Pollack, 622-26 Maccabees Bldg.,
Detroit, Mich.

Place: Wayne County Medical Society. Time: 8:30
p. m., first Wednesday of each month from October
to June, inclusive.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRICS
SECTION (ATLANTA, GA.)

Chairman: Dr. Don F. Cathcart, 478 Peachtree St.
N. E., Atlanta.

Secretary: Dr. Harry Lange, 478 Peachtree St., N. E.,
Atlanta.

Place: Academy of Medicine, 38 Prescott St. N. E.
Time: Second Thursday of each month from October
to April, 8 p. m.

HOUSTON PEDIATRIC SOCIETY

President: Dr. Raymond Cohen, 2300 Caroline St.,
Houston, Texas.

Secretary: Dr. Betty Moody, 526 Richmond Rd.,
Houston, Texas.

Place: College Inn, Houston. Time: Fourth Monday
of each month.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Edwin H. Schorer, 1103 Grand Ave.,
Kansas City.

Secretary: Dr. H. E. Petersen, Kirkpatrick Bldg., St.
Joseph, Mo.

Place: Kansas City General Hospital. Time: On call.

LOS ANGELES COUNTY MEDICAL ASSOCIATION,
PEDIATRIC SECTION

President: Dr. Oscar Reiss, 2200 W. 3d St., Los
Angeles.

Secretary-Treasurer: Dr. Elena Boder, 1830½ Lucille
Ave., Los Angeles.

Place: Los Angeles County Medical Headquarters, 1925
Wilshire Blvd. Time: Second Monday of February,
April, June, October and December.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND
THE ACADEMY OF MEDICINE OF BROOKLYN,
PEDIATRIC SECTION

President: Dr. Abraham M. Litvak, 1145 Eastern Park-
way, Brooklyn.

Secretary: Dr. Harold Levy, 750 St. Marks Ave.,
Brooklyn.

Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m.,
fourth Monday of each month, October to April,
inclusive.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC.,
SECTION ON PEDIATRICS

Chairman: Dr. Meyer Coe, 217-02-91st Ave., Queens
Village, N. Y.

Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th
Ave., Flushing, N. Y.

Place: Queens County Medical Bldg., Forest Hills,
N. Y. Time: Third Monday of October, January,
March and May.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA,
SECTION ON PEDIATRICS

President: Dr. Harry A. Spigel, 2647 Connecticut Ave.,
Washington, D. C.

Secretary-Treasurer: Dr. Perry W. Gard, 2520 Wood-
ley Rd., Washington, D. C.

Place: Medical Society Bldg., 1718 M St. N. W. Time:
8 p. m., fourth Thursday of every month.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. F. T. Mitchell, 376 S. Bellevue Ave.,
Memphis, Tenn.

Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madi-
son Ave., Memphis, Tenn.

Place: John Gaston Hospital. Time: Quarterly.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. John H. Reynolds, 1628 W. Wisconsin
Ave., Milwaukee.

Secretary-Treasurer: Dr. F. J. Mellencamp, 324 E.
Wisconsin Ave., Milwaukee.

Place: Milwaukee Athletic Club. Time: Second Wednes-
day of each alternate month, beginning with February.

NEW YORK ACADEMY OF MEDICINE, SECTION
OF PEDIATRICS

Chairman: Dr. Howard Craig, 175 E. 79th St., New
York.

Secretary: Dr. Alfred E. Fischer, 73 E. 90th St., New
York.

Place: New York Academy of Medicine, 2 E. 103d St.
Time: Second Thursday of each month from October
to May, inclusive, 8:30 p. m.

NORTHERN CALIFORNIA AFFILIATES

President: Dr. Crawford Bost, 400 Post St., San
Francisco.

Secretary: Dr. William A. Reilly, 384 Post St., San
Francisco.

Time: Second Thursday of September, November,
January, March and May.

OKLAHOMA CITY PEDIATRIC SOCIETY

President: Dr. William M. Taylor, 1200 N. Walker
St., Oklahoma City.

Secretary: Dr. G. R. Felts, 625 N. W. 10th St., Okla-
homa City.

Place: Oklahoma Club. Time: Third Thursday of
each month.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Carl Fischer, Greene and Coulter Sts.,
Germantown, Philadelphia.

Secretary: Dr. Sherman Little, 1740 Bainbridge St.,
Philadelphia.

Place: College of Physicians, 19 S. 22d St. Time:
Second Tuesday in January, March, May and
November.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown, Pa.

Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh.

Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Stanley Meace, 913 Floyd Ave., Richmond, Va.

Secretary-Treasurer: Dr. Louise Galvin, 214 S. Boulevard, Richmond, Va.

Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Herbert Soule, 122 Rutgers St., Rochester, N. Y.

Secretary-Treasurer: Dr. Jerome Glaser, 300 S. Goodman St., Rochester, N. Y.

Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Jerome Diamond, 508 N. Grand Ave., St. Louis.

Secretary-Treasurer: Dr. Mary A. McLoon, 408 Humboldt Bldg., St. Louis.

Place: St. Louis Medical Society Bldg. Time: First Friday of each month from November to June.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Frederick B. Joy, Stimson Bldg., Seattle
Secretary: Dr. Sherod M. Billington, Medical Dental Bldg., Seattle.

Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.

Secretary: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.

Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Campbell Harvey, 35 W. Huron St., Pontiac, Mich.

Secretary: Dr. Harry A. Towsley, University of Michigan, Department of Pediatrics and Communicable Diseases, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRICS SECTION (NEW YORK)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.

Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Yonkers, N. Y.

Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.

ANGLE OF CLEARANCE OF THE LEFT VENTRICLE AS AN INDEX TO CARDIAC SIZE

MODIFIED TECHNIC FOR ITS DETERMINATION AND RANGE OF VALUES FOR NORMAL CHILDREN

ROBERT L. JACKSON, M.D.; ROBERT A. J. EINSTEIN, M.D.;
ALICE BLAU, M.D., AND HELEN G. KELLY, M.S.
IOWA CITY

Clinically it is important to detect slight changes in the size and contour of the heart and to try to differentiate between normal and slightly enlarged hearts. Enlargement of the left ventricle occurs frequently with rheumatic heart disease. The present study was undertaken to evaluate one of the quantitative roentgenologic methods used to indicate the size of the left ventricle in children.

Wilson,¹ by determining the degree of rotation necessary to separate the left lower border of the heart (left ventricle) from the vertebral column in fluoroscopic examination in the left anterior oblique position, introduced an index of cardiac size and termed it the angle of clearance. For 97 per cent of 119 normal children ranging in age from 5 to 15 years the angle of clearance was less than 55 degrees; it was between 40 and 45 degrees for 49 per cent, between 45 and 55 degrees for 48 per cent and between 55 and 65 degrees for 3 per cent. Wilson, from her studies, concluded that angles of clearance of 55 degrees or more indicated enlargement of the left ventricle. Fluoroscopic examination in the posterior-anterior position of 119 normal subjects showed the heart to be in the transverse position in 44 per cent of the subjects and in the vertical position in 56 per cent. Hearts that are vertically placed are more likely to have an angle of clearance of 40 to 45 degrees.

Kuttner and Reyersbach,² following the method of Wilson, examined 101 healthy girls ranging in age from 7 to 15 years. For 77 per cent of the children the angle of clearance of the left ventricle was less than 55 degrees; for 21 per cent it was 55 degrees, and for less than 1

per cent it was more than 55 degrees. No definite correlation was found between the angle of clearance and age, body build, height of the diaphragm, position of the heart or state of nutrition. Kuttner and Reyersbach agreed with Wilson that the silhouette of a typically vertically placed heart tends to clear the outline of the vertebral column at a smaller degree of rotation than does that of a transversely placed heart. In view of the number of normal children (21 per cent) for whom the angle of clearance of the left ventricle was 55 degrees, their data suggested that only angles of more than 55 degrees could be considered abnormal. They found that some examinations were unsatisfactory because the children failed to stand properly.

Fluoroscopic examination of the heart in the three standard positions was undertaken in 1941 at the State University of Iowa as part of the routine examination of children with heart disease or suspected heart disease. The examination included the measurement of the angle of clearance as described by Wilson,¹ with the use of a specially made turntable. The only difference between our technic and that of Wilson was that her turntable had fixed points 5 degrees apart. At the various fixed points Wilson viewed the silhouette of the child's heart to obtain the angle at which it cleared that of the spine. The turntable which we used had no fixed points, as we felt that by this means the readings could be obtained more objectively. We rotated the child from the posterior-anterior position (0 degrees) and tabulated the degree of rotation at which the shadow of the heart cleared that of the spine.

Major difficulties soon were encountered in measuring the angle of clearance. We found that the left border of the cardiac silhouette cleared the spinal column at two points: the first, that at which the cardiac border was separated from the projection of the transverse processes of the spinal column, and the second, that at which the cardiac border was separated from the anterior border of the bodies of the vertebrae. There

From the Departments of Pediatrics and Radiology, State University of Iowa, and the State Services for Crippled Children, Children's Hospital.

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2. Kuttner, A. G., and Reyersbach, G.: The Value of Special Radiologic Procedures in Detecting Cardiac Enlargement in Children with Rheumatic Heart Disease, *Am. Heart J.* **18**:213 (Aug.) 1939.

was a difference of approximately 10 degrees between these two points. Frequently it was difficult to duplicate readings for the same child because of minor changes in position. Wilson¹ cautioned against this source of error, and Kuttner² also stated that the examination of some children is unsatisfactory probably as a result of position. We noted that there was a tendency for the children to rotate their bodies from the hip region; so we had them sit rather than stand, to help obviate this source of error.

A new turntable was constructed, which allows the child to sit during the examination (fig. 1). The back rest and the foot rest are adjustable.

The following roentgenoscopic technic has been rigidly adhered to:

1. Examination is done only after adaptation of the eyes to darkness. This necessitates waiting in the darkened room for ten to fifteen minutes or wearing dark goggles for the same length of time.

2. After the entire chest is examined on the screen, the size of the field is decreased so that only the posterior border of the heart is in view. This procedure facilitates differentiation of the landmarks considerably and also minimizes the exposure of the child to roentgen rays.

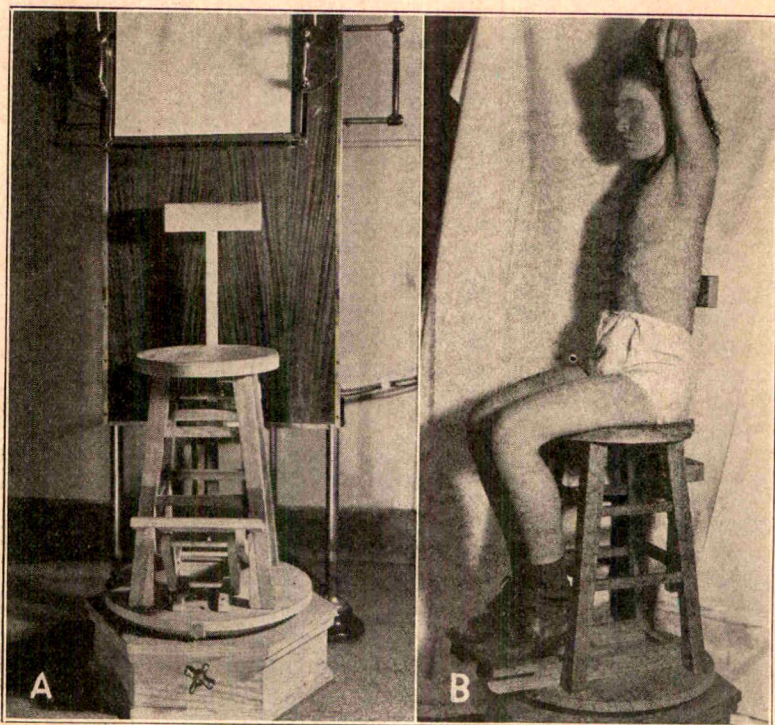


Fig. 1.—*A*, photograph of the modified turntable. The back rest and foot rest are adjustable. *B*, photograph of the turntable rotated to the left anterior oblique position, with the subject sitting in the standardized position.

We place the child on the chair with the arms folded above the head, and he is cautioned to sit erect and motionless. The assistant begins to rotate the chair slowly into the left anterior oblique position while the examiner watches the heart on the fluoroscopic screen. As soon as the posterior border of the heart clears the projection of the transverse processes during normal respiration (fig. 2 *A*), the rotation is stopped and a reading is taken. Then the rotation is continued until the second angle of clearance can be read (fig. 2 *B*).

In addition, the heart is examined in the posteroanterior, right anterior oblique and right lateral positions.

3. The roentgen output of the fluoroscope is measured repeatedly, and special care is taken to reduce the duration of exposure to a minimum. However, we have always observed the heart during both phases of respiration as well as during both cardiac phases.

In order to study the reliability of the angles of clearance, repeated measurements were made for 16 normal children. The number of measurements for each child varied from eight to thirteen. The readings were taken in sets of three or four, and the position was checked but not reestablished for each reading. For this study of reliability no measurement was discarded. From these series of measurements it

as possible to compute a mean angle of clearance for each child and to study the deviations from the separate measurements from the mean value. The assumption is made that the mean value of the repeated measurements of a child is the true angle of clearance.

Table 1 gives for each of 16 children having at least eight repeated measurements the mean, the

ness. Some of the repeated measurements agreed remarkably well, most of them were satisfactory, some were fair and one series was poor. We found it practically impossible to measure one subject (no. 16) without a period of training. The mean deviation of her measurements was 7.0 degrees and 7.5 degrees for the first and second angles of clearance respectively. This 8

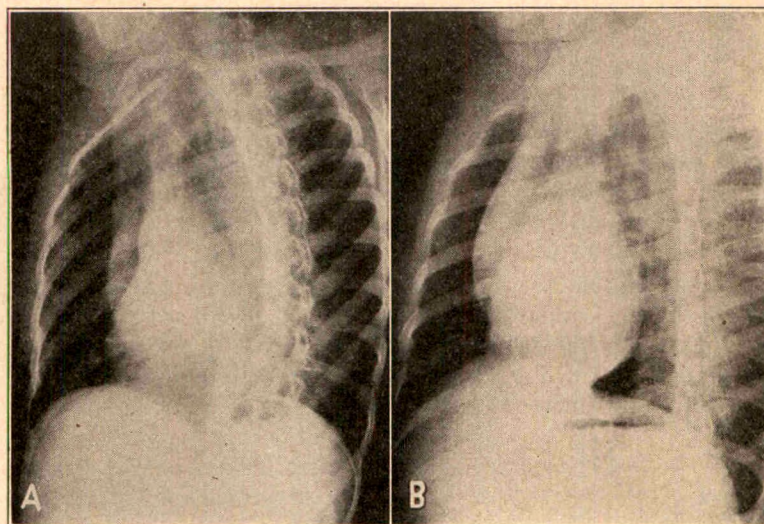


Fig. 2.—Roentgenograms taken with the subject in the left anterior oblique position, *A*, showing the first angle of clearance, with the posterior border of the cardiac silhouette clearing the projection of the transverse processes and *B*, showing the second angle of clearance, with the posterior border of the cardiac silhouette clearing the anterior border of the vertebral bodies.

TABLE 1.—Mean, Standard Deviation, Standard Error of Mean, Mean Deviation and Range of Angles of Clearance for 16 Children

Patient No.	Age, Yr.	Number of Measurements	Mean, Degrees		Standard Deviation, Degrees		Standard Error of Mean, Degrees		Mean Deviation, Degrees		Range, Degrees	
			First Angle	Second Angle	First Angle	Second Angle	First Angle	Second Angle	First Angle	Second Angle	First Angle	Second Angle
1	15	11	60.6	84.9	1.4	3.7	0.4	1.1	1.1	3.0	5	10
2	11	11	57.0	69.8	2.8	2.0	0.8	0.6	2.2	1.5	8	7
3	12	13	42.1	49.7	1.6	1.4	0.4	0.4	1.2	1.2	6	4
4	12	10	43.9	52.4	1.9	2.1	0.6	0.6	1.3	1.7	6	6
5	14	11	52.4	62.6	1.7	2.8	0.5	0.8	1.4	1.8	5	10
6	12	13	53.8	67.2	3.6	4.8	1.0	1.3	3.3	3.9	10	15
7	13	8	56.8	68.9	3.2	3.6	1.1	1.3	2.7	2.9	9	9
8	12	13	58.5	67.8	4.7	4.1	1.3	1.1	3.7	3.0	15	13
9	11	12	65.0	79.8	2.8	2.1	0.8	0.6	2.0	1.8	10	6
10	6	12	51.8	64.5	3.5	2.8	1.0	0.8	3.0	2.3	10	9
11	9	12	50.8	63.6	4.1	4.7	1.2	1.3	3.6	3.8	12	13
12	13	12	54.8	68.8	1.5	1.6	0.4	0.5	1.3	1.3	5	5
13	12	12	51.1	64.6	2.4	3.8	0.7	1.1	1.9	3.3	7	12
14	8	12	54.2	69.2	4.5	4.9	1.3	1.4	3.9	4.3	13	12
15	11	12	52.5	67.3	1.6	1.7	0.5	0.5	1.3	1.3	5	6
16	8	12	53.3	67.0	8.7	10.0	2.5	2.9	7.0	7.5	24	29

standard deviation, the standard error of the mean, the mean deviation and the range for both angles of clearance. For 11 children, 69 per cent of the group, the mean deviation was less than 3.5 degrees for both angles of clearance; for 5 children, 94 per cent, the mean deviation was 3 degrees or less. We were able to measure the angle of clearance of the left ventricle for these 16 children with varying levels of exact-

ness. Some of the repeated measurements agreed remarkably well, most of them were satisfactory, some were fair and one series was poor. We found it practically impossible to measure one subject (no. 16) without a period of training. The mean deviation of her measurements was 7.0 degrees and 7.5 degrees for the first and second angles of clearance respectively. This 8

year old child, though trying to cooperate, unconsciously rotated her body out of the standard position. In reviewing eight series each consisting of twelve measurements taken at three different sittings, it was found that a few sets of measurements showed a bias caused by changes in the position of the child. Changes can occur without the examiner being aware of it, and to elim-

inate the resulting bias, the child should be relaxed between the readings; when he again assumes the correct position, it should be rechecked. By following this procedure the chance of a constant error in the repeated measurements resulting from the fact that the subject held the body slightly rotated or inclined is greatly reduced and the mean of the readings gives a better estimate of the true angle of clearance in the standard position.

We were aware that there were individual differences in the subjects which affected the precision of the measurement of the angles of clearness, but we were interested nevertheless in analyzing the data for the group as a whole. The deviations of the separate measurements from the true values for 15 children were pooled (the data for subject no. 16 were omitted). The average of the deviations of the 174 measurements for the first angle of clearance was 2.3 degrees and for the second angle 2.4 degrees. The standard deviations were 1.8 degrees and 2.1 degrees for the first and the

TABLE 2.—Frequency Distributions of Deviations from the True Values of 174 Measurements of Angle of Clearance for 15 Children

Amount of Deviation (Without Regard to Sign), Degrees	Frequency	
	First Angle	Second Angle
8.5.....	1	1
7.5.....	1	3
6.5.....	2	9
5.5.....	5	2
4.5.....	11	14
3.5.....	18	14
2.5.....	29	26
1.5.....	39	32
0.5.....	43	47
0 to 0.4.....	25	26

second angle of clearance respectively. Judging from these data, not more than 10 per cent of the single measurements vary more than 5 degrees from the true value. Table 2 gives the distribution of the pooled deviations. As stated before, each deviation is the difference between a single measurement of the angle of clearance and the mean of repeated measurements for that child.

We were able to make a limited study of the agreement of measurements made by two radiologists. At one measuring period two radiologists, each working with his trained assistant, secured six paired readings for each of the angles of clearance. It was found that one of the examiners consistently read the first angle of clearance slightly higher than the other examiner and the second angle slightly lower. The mean values of the six paired readings were 59.1 and 57.5 degrees for the first angle and 75.7 and 78.5 degrees for the second angle of clearance.

The difference, of approximately 2.5 degrees, well within the error of the method.

Several factors may influence the precision the measurement of the angle of clearance and cause minor or chance errors. These include (1) slight deviations from the standard position, (2) differences between readings made during the two phases of respiration and the two phases of the cardiac cycle and (3) exactness and ease in determining the landmarks.

It is evident from the data in table 1 that the precision of the measurement depends to some extent on differences in the subjects, chiefly (1) ability to cooperate, (2) ability to sense the correct position and hold it, (3) fatigue and (4) nutritional condition. But unless any of the traits is present adversely in an extreme measure it does not render the examination impracticable.

To study the angle of clearance of children free from cardiac disease, 49 normal boys and 53 normal girls (102 children) ranging in age from 4 to 19 years were examined. Fifteen of the children were hospitalized for metabolic study and twenty-one for conditions not related to heart disease. Sixty-six were children living in Iowa City who were not hospitalized. At the time of the fluoroscopic examination a physical examination of the heart was made, a history of the child pertaining to heart disease and infection of the upper respiratory tract was taken and the height and weight were obtained. On the basis of these data the child was included in or excluded from the group of children free from cardiac disease. Each of the 102 children was examined fluoroscopically on the new turntable and the two points of clearance were read in the manner previously described. The standard position was established and was watched carefully during the measuring period. At least three readings of each angle were made for each child. When an obvious error caused a questionable value, the reading was discarded and another taken. For this group the precaution of relaxing the child between the measurements was not taken. It was subsequent to the time of these measurements that we discovered the bias in repeated measurements caused by changes in position. The final value recorded for the child was the angle of clearance of the left ventricle was the mean value for three measurements.

Before making a statistical analysis of the data we felt we should endeavor to check the extreme values obtained. There were 8 children for whom a first angle over 60 degrees had been recorded. It was possible for 4 of these children to return for a recheck. The angles on recheck were all relatively high, but measurements for 3 of the children were lowered 2 to 7 degrees

and that for the fourth was increased 2 degrees. The highest value obtained was 63 degrees for the first angle and 86 degrees for the second angle. For 2 children angles of clearance of less than 40 degrees were recorded. One child could return for a recheck; her second measurement still was relatively low, but it was raised 9 degrees for the first angle and 11 degrees for the second angle. There must have been an error in position during the first examination of this child.

Table 3 shows the frequency distributions of both of the angles of clearance for 102 normal

TABLE 3.—*Frequency Distribution of Angles of Clearance for 102 Normal Children*

Angle of Clearance, Degrees	Frequency	
	First Angle	Second Angle
85.....	..	2
80.....	..	2
75.....	..	1
70.....	..	12
65.....	2	22
60.....	10	34
55.....	18	21
50.....	45	6
45.....	17	1
40.....	9	..
35 to 39.....	1	..

TABLE 4.—*Mean and Standard Deviation of Angles of Clearance for Normal Boys, for Normal Girls and for Normal Group as a Whole*

	First Angle of Clearance			Second Angle of Clearance		
	Number	Mean, Degrees	Standard Deviation, Degrees	Number	Mean, Degrees	Standard Deviation, Degrees
Boys.....	49	51.4	6.0	49	63.1	7.0
Girls.....	53	52.2	5.3	53	63.2	8.4
Whole group	102	51.8	5.8	102	63.2	7.4

children. The range for the first angle of clearance was from 38 to 67 and for the second from 46 to 86. The mean value for the first angle of clearance (table 4) was 51.8 degrees and for the second 63.2 degrees. The standard deviations were 5.8 and 7.4 degrees respectively.³

The difference between the means of the first and second angles of clearance for the 102 nor-

mal children was 11.4 degrees. There is a high correlation between the first and second angle, and therefore when both are determined they serve as a check on each other.

Our data confirm the observation of Wilson and Kuttner that vertically placed hearts have a lower angle of clearance than transversely placed hearts.

The values for the first angle of clearance were distributed according to build. The data for the subgroups, however, were not sufficient to permit any conclusions. The mean angle of clearance for 33 children who were of average height for their age and average weight for height and age was 52.7 degrees. There was a tendency for fat children to have greater angles of clearance. The mean value for 4 short, fat children was 54 degrees and for 6 fat children of average height 59.3 degrees.

COMMENT

To use effectively any quantitative method to detect slight changes in the size of the heart which occur with rheumatic or other heart disease it is necessary to know the reliability of the method used and the range of normal values. Fluoroscopic examination of the chest is a relatively inexpensive procedure provided the equipment is available. If the angle of clearance of the left ventricle can be measured accurately, a quantitative value for future reference is provided. When the physician uses quantitative values, it is important that he follow a standardized technic.

We followed the principles described by Wilson¹ and by Kuttner and her associates² but altered the method of examination slightly. We found that the new turntable on which subjects are examined while seated allowed less change in position during examination than was observed when the child had to stand. We also found that two points of clearance of the posterior border of the cardiac shadow are easily seen, but also that they might easily be confused. There appears to be a greater difference of contrast between the projection of the transverse process and the surrounding structures than between the anterior border of the vertebra and the neighboring tissues. This appears to facilitate the first reading and therefore to make it more accurate, as is borne out by the smaller range of deviation for that angle.

Inasmuch as we have modified the technic as described by Wilson, our data would not be comparable with those reported by her and by Kuttner. We found wide variation in the angles of clearance for normal children, and we believe that no fixed point should be set below which the readings are considered normal and above which

3. The data for normal children were tested statistically for differences in the means of the angles of clearance for age groups and for sex groups. The slight differences are all well within the limits allowable for chance errors. The means for the angles for the groups according to sex are given in table 4. The mean values for the first and second angles for three age groups are: for 4 to 8 years inclusive, 51.9 and 63.8; for 9 to 11 years inclusive, 52.4 and 63.2, and for 12 to 19 years inclusive, 51.5 and 62.8 degrees.

abnormal. In our opinion it is important to evaluate a subject's angle of clearance in relation to his own repeated measurements as well as in relation to the range of normal values. A reading that is within the normal range might represent an enlarged heart for one child, while it represented a normal heart for another child.

At the present time we are studying the clinical application of the technic described. Frequently a clinician must decide whether a child has cardiac damage or whether active rheumatic heart disease is present. Two of the most helpful signs in making these decisions are the size and the contour of the heart. If the reading for a child with suspected heart disease is within the lower range of the normal values, it is likely that there is no enlargement. If a child has rheumatic fever, one would expect a higher angle of clearance during the active phase of the disease and a gradual decrease of the angle as the patient's condition improves. Repeated examinations showing no significant changes constitute confirmatory evidence that the disease is in the inactive stage. If the angle of clearance remains high, undoubtedly it reflects residual cardiac damage. Conversely, if the angle decreases to a low value it indicates that there is minimal or no enlargement of the left ventricle. If repeated examinations of a child who has had rheumatic fever show no significant change in the readings, the assumption that the disease has remained in the inactive stage receives confirmation.

SUMMARY AND CONCLUSIONS

(1) A modified technic was established for determining the amount of rotation of the subject necessary to make the left lower border of the cardiac silhouette (left ventricle) clear the projection of the transverse processes of the

spinal column (the first angle of clearance) and the left lower border of the cardiac silhouette clear the anterior border of the bodies of the vertebrae (the second angle of clearance) in fluoroscopic examination.

(2) Judging from data obtained by repeated examination to establish the reliability of the method, not more than 10 per cent of the single measurements vary more than 5 degrees from the true value for the subject. For 11 of the 16 children for whom repeated measurement were made, the mean deviation from the true value was less than 3.5 degrees for both angles of clearance.

(3) For 102 normal children examined to determine the normal values, the values for the first angle of clearance ranged from 38 to 60 degrees and for the second angle, from 46 to 80 degrees. The mean value for the first angle of clearance was 51.8 degrees and for the second angle of clearance, 63.2 degrees. The standard deviations were 5.8 and 7.4 degrees respectively. Children with vertically placed hearts showed clearance at a smaller angle than children with transversely placed hearts. There are no significant differences in the angle of clearance of the left ventricle in relation to age or sex. Stocky children tend to have greater than average angles of clearance.

(4) It is our belief that fluoroscopic examination to determine the angles of clearance of the left ventricle is valuable as a supplementary means of studying the heart if the examination can be repeated and the results of subsequent examinations can be compared. Any significant change from the original values could then be interpreted as a change in the size of the heart.

Children's Hospital.

AN UNUSUAL OUTBREAK OF MUMPS

MORRIS SIEGEL, M.D., AND J. L. CAMP, M.D.

NEW YORK

Interest in the control of mumps is usually heightened during wars because of the prevalence of the disease among troops¹ and the consequent danger of outbreaks in crowded civilian groups.

Control based on isolation of patients and quarantine of exposed persons is often ineffective, largely because the infection is highly communicable before the onset of symptoms and the recognition of the disease.²

Efforts to prevent infection by increasing the resistance of susceptible persons have been limited to passive immunization with convalescent blood or serum.³ The results of such measures have varied greatly. Although many investigators have reported protection of all or almost all of the persons inoculated,⁴ some have had a sufficiently large percentage of failures to introduce doubt as to the prophylactic value of the procedures employed.⁵ These differences are not

easily explained.⁶ They reflect the existence of variables which make interpretation of the results of clinical studies difficult.

An unusual institutional outbreak of mumps revealed the extent to which uncontrolled conditions may vary and showed the need for adequately chosen controls in evaluating clinical data on prophylaxis. The outbreak occurred at Letchworth Village, a New York State institution for feeble-minded persons. It developed among boys residing in eight cottages (A, B, C, D, E, F, G and H). Each cottage housed 80 to 90 inmates and 8 employees. Cottages A and F had mainly adolescent boys and young adults who were engaged in various occupations throughout the institution. Cottages B, C, D and E were occupied mainly by children of school age who intermingled each day except Saturday and Sunday in classrooms and workshops. Cottages G and H housed inmates of low grade intelligence who were confined to their respective cottages or were allowed limited activities out of doors. The inmates of cottages A, B, C and D used one common dining room, and those of E, F, G and H, another.

The number of inmates susceptible to mumps was unknown. None had been previously exposed to the disease at the institution. With few exceptions they were from urban areas, and about 85 per cent of them were from New York city. They were comparable physically to the general population. The age distribution of the inmates by cottages is shown in table 1.

There was close contact between persons who were inmates in the same cottage. They lived together like one family. The sleeping quarters in each cottage were limited to two dormitories,

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each with about forty beds, arranged in three rows, with about 12 inches (30 cm.) of space between adjacent beds and 5 feet (150 cm.) between the rows.

Newly admitted inmates were confined to their respective cottages for the first few days except at meal times, when they were in contact with inmates of other cottages using the same dining room.

Mumps was introduced into the group by an inmate who entered the institution during the incubation period. He was admitted on March 8 at 11 a. m. and was sent at once to cottage B, where he remained for twenty-four hours. On March 9 at about 10:30 a. m. he was transferred to cottage E. That evening, about ten hours after admission to cottage E, he complained of earache. Enlargement of the glands was not noticed at this time. The following morning

TABLE 1.—*Age Distribution of the Inmates by Cottages*

Cottage	Total Number of Inmates	Age, Years			
		4 to 9	10 to 14	15 to 19	20 and Over
A	84	0	0	43	41
B	85	37	38	4	6
C	81	1	51	24	5
D	80	1	42	34	3
E	88	6	67	11	4
F	88	1	10	67	10
G	86	0	29	54	3
H	85	23	41	12	9
Total	677	69	278	249	81

(March 10), after he had been in cottage E for twenty-four hours, swelling of the left parotid gland was evident and a diagnosis of mumps was made. He was put to bed in his dormitory and remained in cottage E during his entire illness.

Since there had been no cases of mumps at the institution for a few years, an extensive outbreak was expected. Therefore a question arose as to the advisability of employing convalescent serum in an effort to protect the exposed inmates, particularly those in cottage E, where the infected patient was staying. It was decided not to use serum because the amount available was not sufficient for all the inmates, or even for half of those in cottage E if a controlled test of its efficacy was planned.

Twenty-one secondary cases of mumps occurred from March 25 to April 4, 20 in cottage B, where the infected patient had stayed for twenty-four hours shortly before the onset of his symptoms, and 1 in cottage D as a result of exposure in the dining room. During this period no secondary cases occurred in cottage E, where many were expected because the inmates were exposed to the first patient shortly before the onset of symptoms and throughout the illness.

The date of onset of symptoms and the length of the incubation period for the 21 secondary cases are shown in table 2.

After the inmates had been exposed to the secondarily infected patients, 21 additional cases occurred between April 11 and April 22. The dates of onset for the new cases and the distribution by cottages are shown in table 3.

TABLE 2.—*Date of Onset and Incubation Period for Twenty-One Secondary Cases*

Date of Onset	Incubation Period, Days	Number of Cases
3/25.....	16-17	1
3/26.....	17-18	0
3/27.....	18-19	5
3/28.....	19-20	4*
3/29.....	20-21	3
3/30.....	21-22	0
3/31.....	22-23	4
4/1.....	23-24	2
4/2.....	24-25	1
4/3.....	25-26	0
4/4.....	26-27	1
Total.....	18-27	21

* One case in cottage D, all others in cottage B.

TABLE 3.—*Dates of Onset of New Cases and Distribution by Cottages*

Date of Onset	Number of Cases	Cottage
4/11.....	1	B
4/12.....	2*	B
4/13.....	4*	B
4/14.....	1	B
4/15.....	1	D
4/16.....	1	D
4/17.....	1	D
4/18.....	3	C
4/19.....	4	C, D†
4/20.....	1*	C
4/21.....	1	D
4/22.....	1	D

* Includes a case in which the patient was an attendant.
† Two cases in cottage C and 2 cases in cottage D.

The first 8 cases of the second wave of the epidemic occurred between April 11 and April 14 in cottage B, where there was intimate exposure to 20 patients; the next 3 developed between April 15 and April 17 in cottage D, where there was exposure to 1 patient, and the last 10 occurred in cottages D and C, whose inmates used the same dining room and school. No cases occurred in cottage E, despite exposure of the inmates at school and in the workshops.

After April 22, there were only 2 new cases. One occurred in cottage E; it was the first to occur there since the primary case was discovered. The date of onset for this case was May 2 and for the other, May 9. The last patient was an attendant in cottage C.

A summary of the development of secondary cases and the cottages in which they occurred is presented in table 4.

Forty inmates and 4 employees in cottages B, C, D and E had mumps during the epidemic. Only 1 person in cottage E acquired the disease, toward the end of the outbreak, even though its occupants had been in contact with primary and secondary sources of the infection in various stages of the disease.

The age-specific rates for cottages B, C, D and E combined are shown in table 5.

TABLE 4.—*Dates of Onset for Secondary Cases and Distribution by Cottages*

Date of Onset	Number of Cases	Distribution of Cases by Cottages			
		B	C	D	E
3/25 to 4/ 4	21	20	0	1	0
4/11 to 4/22	21(8)*	8(2)	6(1)	7	0
5/ 2 to 5/ 9	2(1)	0	1(1)	0	1
Total.....	44(4)	28(2)	7(2)	8	1

* Figures in parentheses indicate the number of cases in which the patient was an employee.

TABLE 5.—*Age-Specific Rates for Cottages B, C, D and E Combined*

Age, Yr.	Number of Inmates Exposed	Inmates with Mumps	
		Number	Per Cent
Under 10.....	45	11	24.4
10 to 14.....	198	26	13.1
15 to 19.....	73	3	4.1
20 to 29.....	18	0	0.0
Total.....	334	40	12.0

TABLE 6.—*Comparison of Observed and Expected Incidences of Mumps in Cottage E*

Age of Inmates, Yr.	Number of Inmates in Cottage E	Number of Inmates with Mumps	
		Expected	Observed
Under 10.....	6	1.5	0
10 to 14.....	67	8.8	1
15 to 19.....	11	0.5	0
20 to 29.....	4	0.0	0
Total.....	88	10.8	1
Per cent.....	..	12.3	1.1

If the same rates applied to the inmates in cottage E, a greater number of patients than that observed would be expected there (table 6). The expected incidence was 11 times greater than the observed incidence.

The difference between the observed and the expected incidence of mumps in cottage E is increased if the age-specific rates for cottage B, where the first patient stayed for twenty-four hours prior to his transfer to E, are applied. The incidence attributable to direct exposure to the first patient alone is shown in table 7. As many as 24 (26.8 per cent) secondary cases of mumps were to be expected in cottage E if all the conditions in E were the same as those in B.

The number of expected cases is increased to 31 if those resulting from exposure to secondarily infected patients in B are included, as shown in table 8. On this basis the number of cases expected in cottage E was 31 times greater than the number observed.

Data on the incidence of various contagious diseases of childhood were obtained during the ensuing year during outbreaks of measles, rubella, whooping cough and chickenpox at the institution.⁷ The incidence of these diseases and of mumps in cottages B, C, D and E are shown in table 9.

TABLE 7.—*Incidence of Mumps Attributable to Direct Exposure to the First Patient*

Age Group, Yr.	Cottage B			Cottage E		
	Inmates	Inmates with Mumps		Inmates	Inmates with Mumps	
		No.	Per Cent		Expected	Observed
Under 10	37	8	21.6	6	1.3	0
10 to 19	42	12	28.6	78	22.3	0
20 to 29	6	0	0.0	4	0.0	0
Total	85	20	23.5	88	23.6	0
Per cent.....					26.8	

TABLE 8.—*Incidence of Mumps in Cottage B and Expected and Observed Incidences in Cottage E*

Age Group, Yr.	Cottage B				Cottage E		
	Number of Inmates	Inmates with Mumps		Number of Inmates	Inmates with Mumps		
		No.	Per Cent		Expected	Observed	
Under 10	37	10	27.0	6	1.6	0	
10 to 19	42	16	38.1	78	29.7	1	
20 to 29	6	0	0.0	4	0.0	0	
Total	85	26	30.6	88	31.3	1	
Per cent.....					35.6	1.1	

Rates were uniformly highest for cottage B and next highest for E, with the exception of mumps, for which the rate was lowest for E. On the whole, the rates for E were well above the average for measles, rubella and chickenpox and almost average for whooping cough. On this basis, the incidence of mumps in E would be expected to be equal to or somewhat above average instead of significantly below average.

COMMENT

An outbreak of mumps has been described in which the incidence of the disease in four cottages (B, C, D and E) ranged from 1 per

7. The epidemics considered in the present report occurred on the following dates: Mumps, 3/25/40 to 5/9/40; chickenpox, 9/7/40 to 2/6/41; whooping cough, 10/20/40 to 11/24/40; measles, 2/28/41 to 3/26/41, and rubella, 5/13/41 to 6/14/41.

cent to 31 per cent. It was lowest in cottage E, in which many cases were expected because the 88 inmates had been intimately exposed to patients in various stages of the disease and because of the relatively high incidence of other contagious diseases of childhood exhibited in the group. Actually no case occurred there until eight weeks after the primary exposure, and then only 1 occurred. Depending on the method of calculation, the number of cases expected in cottage E was from 11 to 31 times greater than the number observed. If these results had been obtained after the use of convalescent serum in cottage E, they might have been presented as clearcut evidence of perfect prophylaxis. The single occurrence eight weeks after the onset of exposure might have been attributed to the return of susceptibility in a passively immunized child. In addition, data obtained during epidemics of other communicable diseases that

of clinical infections failed to occur. This might occur in a disease like mumps, with a short period of infectiousness which reaches its height about twenty-four hours before the onset of symptoms. Under such conditions the affected child might infect in high degree a host of persons within the last twenty-four hours before clinical symptoms appeared and become relatively innocuous shortly after that.

While this explanation seems plausible for the occurrence of many secondary cases in cottage C and the absence of secondary cases in cottage D after exposure of the inmates to the first patient it does not explain the lack of clinical infection despite repeated contact with secondarily infected inmates in all stages of the disease. During the later stage of the epidemic there was probably considerable exposure to the infectious agent. Yet only one clinical infection developed in an inmate of cottage E. It therefore seems

TABLE 9.—Incidences of Various Contagious Diseases for Cottages B, C, D and E

Cottage	Population	Measles		Rubella		Whooping Cough		Chickenpox		Mumps	
		Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
B.....	85	40	47.1	20	23.5	22	25.9	6	7.1	26	30.6
C.....	81	10	12.3	4	4.9	2	2.5	0	0.0	5	6.2
D.....	80	3	3.8	0	0.0	1	1.3	1	1.3	8	10.0
E.....	88	20	22.7	13	14.8	6	6.8	4	4.5	1	1.1
Total.....	334	73	18.7	37	8.5	31	7.1	11	2.5	40	9.2

occurred during the year might have been used to support the evidence that the children in cottage E were "protected" against mumps, because it was only for this disease that the incidence in cottage E was significantly lower than the average. Only the use of controls in cottage E would have indicated that either no cases or only 1 should have been expected there under the prevailing conditions. The use of any other controls, such as persons in a different cottage, as for example cottage B, would have been misleading, even though the children lived at the same institution under comparable conditions.

The unexpectedly low incidence of mumps in cottage E was due to some anomalous condition there, either in the degree of exposure to the infection or in the number of susceptible persons in the group. If one considers the incidence of the communicable diseases of which epidemics occurred shortly after the outbreak of mumps and the randomness in the distribution of children among the various cottages, it seems highly improbable that there were few susceptible persons in cottage E. It seems more likely that the susceptible children were inadequately exposed and that therefore the expected number

that either there were fewer susceptible children in cottage E than expected or that the susceptible children there were naturally protected in some undetermined way. Such protection could be induced by subclinical infections caused by exposure to the first patient after he was transferred to cottage E, at a time when his infectiousness was low. The long incubation period would allow sufficient time for immunologic changes to occur. The degree of immunity arising from subclinical infection during the early part of the epidemic would be sufficient to protect against clinical infection from intimate contact with infected persons later on. The role of inapparent infection in protecting susceptible persons against bacterial and virus diseases is widely accepted. In mumps this form of "symptomless immunization"⁸ has been experimentally produced by the inoculation of "small quantities of virus" in

8. (a) Footnote 2. (b) Gordon, J. E., and Heeren, R. H.: The Epidemiology of Mumps, *Am. J. M. Sc.* 200:412-428 (Sept.) 1940.

9. Topley, W. W. C., and Wilson, G. S.: The Principles of Bacteriology and Immunity, ed. 2, London, Edward Arnold & Co., 1936.

Macaca rhesus.^{5d} Its occurrence in man is likely, since a large part of the population in endemic areas never acquires the disease and about 50 per cent of persons with no history of mumps have complement-fixing antibodies and positive cutaneous reactions indicative of past infection.¹⁰

However one interprets the unusual data in this article, the record of what happened when mumps was introduced into Letchworth Village demonstrates the extent to which the disease can be disseminated before its recognition and the pitfalls of a clinical investigation that is inadequately controlled or dependent on a single trial.

10. (a) Enders, J. F., and Cohen, S.: Detection of Antibody by Complement-Fixation in Sera of Man and Monkey Convalescent from Mumps, *Proc. Soc. Exper. Biol. & Med.* **50**:180-184 (May) 1942. (b) Enders, J. F.: Observation on Immunity in Mumps, *Ann. Int. Med.* **18**:1015-1019 (June) 1943.

SUMMARY

In an outbreak of mumps at an institution the incidence of the disease in one cottage was significantly lower than would be expected on the basis of the incidence in other cottages and in epidemics of other contagious diseases. The experience illustrates how a single trial of a prophylactic measure may be erroneously interpreted in the absence of adequate controls.

NOTE.—After the 1940 epidemic herein described, no new cases of mumps were observed at the institution until July 16, 1944, when a second outbreak occurred. It affected 11 inmates, 8 in cottage B, and 1 each in cottages C, D and E. Since all who acquired the disease were admitted to the institution after the 1940 epidemic, the indications are that the persons exposed in 1940 are now immune.

Foot of East Fifteenth Street.

SIGNIFICANCE OF A COMPLETE PREVENTIVE MEDICAL PROGRAM FOR CHILDREN

C. ANDERSON ALDRICH, M.D.

ROCHESTER, MINN.

A former public health official from an occupied country in Europe said to me the other day: "We have been educating for this war for forty years! The way we have cared for our babies and young children has encouraged the kind of personality that makes violent conflicts inevitable." "Types like Hitler and Mussolini," he went on, "must be expected to develop when we deny to children the secure personal background necessary for normal growth."

This physician was greatly impressed with the possibilities for human development that might be offered by a community medical program which would take into account, from the first days of a child's life, not only his physical health and welfare but his basic emotional needs as well. This is the kind of program to which the Rochester Child Health Project looks forward.

DEVELOPMENT OF PEDIATRIC THOUGHT

Before going into the plan I should like to digress for a few minutes to sketch the background of this project. Pediatricians are responsible for some of the lacks and failures in the field of child care today, as well as for its evident successes. Therefore, a review of pediatric thought since its beginnings, about fifty years ago, may help toward an understanding of how interest in this more comprehensive type of program arose.

This medical specialty started as a separate division devoted to "diseases of children," and was made necessary by the alarming mortality among infants during the late eighteen hundreds. Diphtheria, tuberculosis, intestinal disorders, infectious disease and contamination of milk and water supplies were acute problems which had to be solved, since at that time mortality statistics indicated the death of about 1 of every 4 babies in the first year of life. The effort to improve this situation furnishes one of the bright chapters of medical history, and the scientific management of the children built up for this branch of medicine a well deserved prestige.

As time went on, this supposedly health-bringing program for the care of children grew

to be in many cases a meticulous and burdensome regimen. Medical ideas were learned at that time by study in Austria and Germany; routines planned with continental efficiency gradually became rigid schedules that had little relation to the reality of a growing child.

Only a few years ago exacting schedules were being imposed on mothers and children, and the aftermath still persists. Formulas calculated to the ounce were prescribed, and mothers were encouraged not to "give in" to their babies—to let them cry it out if the clock had not yet reached the proper hour for feeding or bath. The behavioristic psychologists made matters worse by their theory that fondling, rocking or singing to a child spoiled him—that the mother who devoted herself to such softening measures would make her son a mamma's boy and a sissy. All the natural motherly emotions were tabooed along with grandmother's rocking chair. In the name of science a long step was taken against nature's laws.

But science is really an attempt to interpret nature. When the spirit became lost in the letter of the law, science became unscientific and the children suffered, not in the old way but in a new way—through disturbances of behavior and failure to conform to the arbitrary daily standards set up for them. Problems of feeding, sleeping and elimination multiplied, and tantrums flourished, in spite of the best intentions of physicians and parents.

All this would not have happened had pediatricians known what they know today about normal growth and development. But unfortunately the results of scientific research do not all come at the same time. Physicians have to act in the light of what they know today, not in the light of what they will know tomorrow. They learned about nutrition and calories before they found out about normal growth. This important piece of the picture puzzle was lacking and is just beginning to be fitted in now.

Science does change when confronted with facts—and a great many facts have been coming along during the past twenty years.

As is well known, a great deal of work has been done in the psychologic field to sift the fac-

From the Rochester Child Health Project, Section on Pediatrics, the Mayo Clinic.

ors in a child's early environment, to determine which are helpful and which are obstructive or disturbing.

Educators in the schools have also been applying scientific methods to the curriculum and are finding that various subjects can be taught more efficiently when the mental development of a child has reached a definitely appropriate stage. It is now recognized, for instance, that the ability to read is a developmental step and that before eye and brain are set for this accomplishment in the individual child he cannot learn to read well. To know more about the stages of mental development is one of the goals of educational research today.

Most significant of all, perhaps, the steps in physical growth are being studied intensively and are yielding a new yardstick for the evaluation of the care of children. Such research, notably that carried on in the laboratory of Dr. Arnold Gesell, The Clinic of Child Development, Yale University has revealed two important facts. First, there is a startling uniformity in the sequence of the stages in human development; for instance, practically all babies sit up, crawl, stand and walk in this sequence. Second, the stages of a child's growth can be predicted accurately from month to month.

On the basis of these facts, a developmental schedule of growth can be plotted which is applicable to all children; although the rate of growth varies. For instance, it is known that an average normal baby will smile at about 6 weeks, will be able to reach out for objects with both hands at approximately 4 months, will develop pincer movements of the fingers and thumb at 9 to 11 months and will be able to attain control of the bladder in the second year.

The importance of these simple discoveries cannot be overemphasized, because when their implications sank in it was realized that the early formation of habits of eating, sleeping and elimination, as well as the early acquisition of motor skills, was more dependent on the maturation of the child than on attempts to teach him. It then appeared logical that he could be taught each act most easily when the appropriate developmental stage had been reached. The whole scheme of early education became simpler when a detailed knowledge of normal growth and development was applied to each problem.

With this background it has come to be realized that many of the problems in personality that parents have faced with children have arisen because the parents failed to adjust the care of their children to the newly discovered facts of growth. Young children have been expected to behave in ways for which they were not yet ready. Most parents, for instance, have tried to

make them eat from spoons before the muscles of their tongues and lip had developed properly. Parents have tried to "train" children against the current of their natural development. This is illustrated repeatedly in premature attempts to train for control of the bowel and the bladder.

As a result, many children have become confused, resistant and subject to emotional storms. Such children are called "spoiled." They have really been misfitted. Obviously the adults must do some revamping of their methods, so that the care of children can be based on the actual needs of growth rather than on arbitrary standards.

What are these needs of growth? Not all of them are known. No one knows all the secrets of the care of children any more than those of farming or of animal husbandry. But those who constantly observe children feel that they do know some of these secrets. Every one agrees that children need fresh air, sunshine, adequate clothing, food and sleep. These physical needs are conscientiously included in every program for nursery care, including that of the Rochester Child Health Project.

But there are other things which have come to be recognized as equally important. Modern babies apparently need a closer contact with their mothers during the first few weeks of life than they are usually allowed. They also need a more individual program: to be fed, for instance, by their own feeding schedules (for every baby has a feeding schedule, if one takes the trouble to find it). In fact, children need to be allowed to use each new ability as it appears: to feed themselves, for instance, as soon as they are able to manipulate a spoon; to walk and climb as they begin to get their equilibrium. For it is in these simple nursery activities that there begins to develop the sense of confidence and competency which every one recognizes as vital to later success.

THE ROCHESTER CHILD HEALTH PROJECT

So much for the background of the Rochester Child Health Project. The project itself has two main objectives: first, to offer all the children of Rochester supervision of health based on the needs of the individual child for optimal growth; second, to study the growth of these children from conception to maturity by means of continuous observation and records. It will be a valuable piece of research in itself to see whether a community can be interested in such a program.

It should be mentioned that Rochester, Minn., a city of about 30,000, provides an unusual opportunity for this sort of program. Practically

all of the children born in the city are under uniform medical supervision. Ninety-five per cent of them are born in one hospital, under the care of the obstetricians of the clinic, and are seen in the home and in the neonatal and the well baby stations by the pediatricians of the clinic.

The project is fortunate also in having the full cooperation and support of the city public health officers, of the city medical, nursing and social service agencies and of the executive officers of the city schools. The school system and the health department already have a well coordinated health program and are ready to consider the present project as one more phase of their work. Thus the project has a unique backlog of help and interest from persons and agencies in the city. I feel, with my associates in the project, that this wholehearted assistance from citizens of Rochester will go far toward making our objectives possible.

We intend to begin with the babies born in 1944, trying to set the environment favorably as they progress through the years. As we picture the organization of the project at the time of writing, there will be five principal types of care, each adapted to a different age group.

The Antepartum Clinic.—In this clinic we shall be interested not only in the diet and physical hygiene of the mother but in her attitude toward the coming baby. She and her husband will be encouraged to learn what a newborn baby is like, what the baby will need from them, why breast feeding is important and how to prepare their home for the advent of the new inmate.

At present we propose to offer this education partly by means of classes, partly by individual talks at conferences and partly by a series of leaflets to be filed by the mother in a loose leaf folder. During the early years this folder will also be used to summarize the measurements of growth and to preserve a record of illnesses, immunizations and any other facts of interest in regard to health.

Hospital Care.—During the mother's stay in the hospital after the birth of the baby, every effort will be made to give both baby and mother not only good physical care but a satisfying and comfortable time together, and to institute breast feeding of as high a percentage of babies as possible.

It is anticipated that the technic of caring for newborn babies will have to be studied and modified considerably, and to that end we are now making plans. For instance, on dismissal to go home the mother is instructed not to be afraid to pick up her baby when he cries unduly, and she is told that rocking chairs are back in style. Most

of the modern young mothers are surprised and relieved to learn that they can be motherly.

Well Baby Clinic.—Continuing at the well baby clinic, the baby will be seen at least once a month or oftener if necessary for a check-up of feeding, general supervision of health and inoculation against contagious diseases. The mother and the father will also be offered a chance at these conferences to learn more about the social development and the formation of habits in the baby. This teaching will be based on study of growth and development.

Preschool Clinic.—Less frequent follow-up in a formal clinic is expected for the preschool child. Probably some of the work will be carried on through the education of small groups of mothers and children from the same neighborhood, supervised by trained nursery school workers. One or two nursery schools will be organized as demonstration centers. During these years we expect to continue our interest in growth and development as they affect the formation of habits and the social interests of children. We hope also to prepare mother and the child for the public school, so that the children will retain the natural desire to learn and will preserve the sense of adequacy which we have tried to foster during their early years.

School Health Program.—We shall try to protect children from undue incidence of disease by routine examinations and by supervision of health. We also hope to continue the study of growth and development in cooperation with the teaching program so that the utmost abilities of the individual pupils may be utilized as they grow.

RESEARCH

It is natural that out of such a program should come many questions. Research, therefore, will be an inevitable part of our activities.

Already we are devoting considerable time to an attempt to understand why babies cry and to learn how to prevent excessive crying both during the period spent in the hospital and after the babies go home.

At present, in spite of every care, the highest human mortality occurs in the first two weeks of life. We are trying to collect facts which will help us better to meet the physiologic needs of these young children at a critical stage of their growth.

Research has also been started to see whether it is possible to correlate the muscular tension of newborn infants with their emotional behavior. We expect to carry these observations on as the children grow up, in order to discover whether dynamic personality is a native characteristic and whether it can be recognized at birth.

Obviously there will accumulate a file of histories of many of the children in the community. Summaries of the salient points in these histories are being made by means of a punch card system of records so that they may be easily collected at any time for study.

It is anticipated that while we shall keep some records of measurements of growth, this phase of our research will not be emphasized. Equal attention will be given to the mental and emotional development of the children under our care.

APPLICATION

This means that we shall be especially interested in preventing disturbances of behavior and in encouraging each child to develop his own best possibilities.

This approach to problems of behavior—attacking them through early prevention rather than through later treatment in child guidance clinics—is a fundamental part of our project. It would be impossible to set up the machinery necessary to treat successfully all the unhappy and mishandled children of any community, because of the number of such children. We are interested in finding out whether, by mass education as to prevention, we can obtain a better result, with less expenditure of time and money, than has been obtained under existing methods.

This seems to us a practical objective, since mental disease is one of the major problems of the present time.

It is understood that only the broad aspects of mental health can be touched by such a program. Economic factors, hereditary tendencies and the complexity and confusion of the present world are bound to create stresses, but it will be interesting to see how many children brought up in a community where parents understand the implications of normal growth will get the basic confidence needed to meet these strains. •

We feel too that we should be interested, and we are interested, in a still wider aspect of the development of the community. An effort at promoting the growth of the individual must have some relation to democratic citizenship. The children now growing up will be the leaders of the future. Successful leaders in a democracy must be emotionally stable enough to stand on their feet and to give and take with their neighbors. This emotional stability must stem from a basic security and confidence, the kind that grows up from childhood. It does not seem impossible that human nature may have more potentialities for cooperation than has hitherto been believed. A start at testing these possibilities can be made by applying the wholesome principles of growth to the care of children.

PREPARATION AND IMMUNIZING PROPERTIES OF PROTAMINE DIPHTHERIA TOXOID

VICTOR ROSS, PH.D.

NEW YORK

Alum-precipitated diphtheria toxoid is antigenically superior to "fluid" toxoid, since it elicits a higher titer of antitoxin when equal quantities (Lf) are injected. Fewer injections are consequently needed to produce a satisfactory immunity against diphtheria. However, both in adults and in adolescents its use frequently results in disagreeable reactions, largely local but occasionally systemic. There has been, therefore, a tendency to return to the use of "fluid" toxoid, even though it involves the extra burden of additional injections. Even this preparation produces in some adults reactions which are so annoying that the immunization may not be carried to completion. This eventuality may be avoided by resorting to very small doses of toxoid, but the objection to this method is the length of time it takes to administer the total volume required. The reactions are ascribed partly to bacterial body protein which goes into solution in the course of the autolysis of some of the diphtheria bacilli and partly to the proteins used in preparing the broth for growing the organisms. These substances are in part precipitated along with the toxoid when alum is added to the solution. Finally, it is believed that some persons are sensitive to the toxoid itself.

It occurred to the writer that diphtheria toxoid might be precipitable by protamine and that such a precipitate might possess the immunizing advantages of alum-precipitated toxoid and yet not give rise to the undesirable reactions that the latter preparation sometimes produces in adults and in older children. This procedure has been tried, and it has been found that diphtheria toxoid can be precipitated by protamine and that the precipitate will immunize guinea pigs and human beings. It produces only slight erythema and induration in children: About 2,600 children have been immunized with 1 cc. of the new

preparation without a single child's having become ill. In adults the reactions are qualitatively the same but quantitatively greater: Even when erythema and induration were largest interference with motion of the arm did not take place. A rise in body temperature occurred infrequently (in 3 adults who were extremely sensitive as judged by the "reactor" test). The number of adults that have been inoculated is not yet large enough to justify omitting the "reactor," or "sensitivity," test before deciding on the quantity to be injected.

The experimental data will be presented under the following headings: (1) preparation of the protamine toxoid, (2) reactions following intradermal injection of equivalent quantities of the new preparation and of alum-precipitated and of "fluid" toxoid in adults, (3) immunizing properties as determined in guinea pigs and (4) reactions and immune response following subcutaneous injection in (a) adults and (b) children.

PREPARATION OF PROTAMINE TOXOID

To each cubic centimeter of diphtheria toxoid made with veal extract there are added 10 mg. of sodium chloride and 3.5 mg. of protamine sulfate, the protamine component of which is derived from sperm of mature testes of fish belonging to the family Salmonidae. The quantities of sodium chloride and of protamine sulfate may vary with different lots of "fluid" toxoid. The mixture is allowed to stand for two days at room temperature and is then centrifuged. The bacterial body protein is precipitated along with some broth protein, while the toxoid remains in solution. To the supernate is added three volumes of distilled water. The protamine toxoid appears in an extremely fine state of subdivision. After one hour 1 cc. of a 0.4 per cent solution of potassium alum ($\text{KA1}[\text{SO}_4]_2 \cdot 12\text{H}_2\text{O}$) is added for every 10 cc. of the suspension. This adsorbs the precipitate, which then settles rapidly. The sediment is washed with isotonic solution of sodium chloride and resuspended in a volume of salt solution equal to that of the original toxoid. Sufficient sodium ethyl mercurithiosalicylate is added to make 1 part in 7,500. There are 150 or more flocculating units per milligram of nitrogen

From the Department of Biochemistry, College of Physicians and Surgeons, Columbia University.

This study was financially aided by Lederle Laboratories, Inc., Pearl River, N. Y., Dr. W. G. Malcolm, Director.

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in such a preparation. This nitrogen includes that derived from the protamine, estimated at about one-half the total. Therefore, the ratio of coagulating units to milligrams of broth nitrogen is about 300 to 1.

COMPARATIVE REACTIONS PRODUCED BY INTRADERMAL INJECTION OF PROTAMINE TOXOID, ALUM-PRECIPITATED TOXOID AND "FLUID" TOXOID

A 1 to 10 dilution of protamine toxoid and one of alum-precipitated toxoid were prepared in isotonic solution of sodium chloride, and 0.02 cc. of each was injected intradermally into the forearm of each of 18 adults whose ages ranged from 21 to 28 years. The arms were examined after twenty-four and forty-eight hours, and measurements were made of the areas of erythema. In every instance the alum-precipitated toxoid produced a central redder area and an outer, less intensely red, area. The protamine toxoid produced two zones in about one half of the subjects and only one zone in the rest. In every case the total area of erythema was very much greater at the site of the injection of the alum-precipitated toxoid. Table 1 shows that the smallest ratio of the area of erythema produced by alum-precipitated toxoid to that pro-

TABLE 1.—*Erythema Produced by Intradermal Injection of 0.02 Cc. of a 1 to 10 Dilution of Protamine Toxoid and of Alum-Precipitated Toxoid (Diphtheria) in Adults*

Subject	Protamine Toxoid Erythema (in Mm.)		Alum-Precipitated Toxoid Erythema (in Mm.)	
	After 24 Hr.	After 48 Hr.	After 24 Hr.	After 48 Hr.
1	12 × 7	5 × 3	22 × 20	17 × 15
2	2 × 3	4 × 2	12 × 16	10 × 15
3	5 × 2	0	10 × 10	20 × 4
4	6 × 4	3 × 3	13 × 13	12 × 11
5	11 × 7	15 × 15	30 × 32	45 × 35
6	10 × 7	6 × 4	25 × 22	32 × 35
7	7 × 8	16 × 13	18 × 18	25 × 35
8	3 × 2	2 × 2	14 × 16	10 × 18
9	5 × 6	4 × 3	15 × 25	6 × 7
10	13 × 13	26 × 22	25 × 16	35 × 38
11	13 × 23	31 × 26	30 × 40	55 × 32
12	6 × 4	4 × 4	11 × 13	5 × 6
13	5 × 5	4 × 4	32 × 40	28 × 38
14	15 × 20	14 × 26	25 × 23	37 × 35
15	2 × 1	0	9 × 9	5 × 2
16	2 × 1	0	22 × 16	7 × 4
17	10 × 6	5 × 2	20 × 28	10 × 11
18	5 × 6	5 × 6	15 × 15	9 × 18

duced by protamine toxoid was 4 and the largest ratio 50.¹ Also, the intensity of redness was considerably greater with the alum-precipitated toxoid.

Table 2 shows the results of intradermal injection of a 1 to 10 dilution of protamine toxoid and of a 1 to 20^{1a} dilution of the regular "fluid" toxoid. The ratio of the respective volumes injected was different in each of three groups

of subjects and is indicated in the table. Arms were examined after twenty-four and forty-eight hours and in some instances after seventy-two hours as well. For equal quantities (Lf units) of toxoid (subjects 30 to 35) the areas of erythema produced by the "fluid" toxoid customarily

TABLE 2.—*Erythema Produced by Intradermal Injection of a 1 to 10 Dilution of Protamine Toxoid and of a 1 to 20 Dilution of "Fluid" Toxoid (Diphtheria) in Adults*

Subject	Protamine Toxoid* Erythema (in Mm.)			"Fluid" Toxoid* Erythema (in Mm.)		
	After 24 Hr.	After 48 Hr.	After 72 Hr.	After 24 Hr.	After 48 Hr.	After 72 Hr.
19	5 × 5	5 × 4	5 × 4	10 × 11	40 × 21	19 × 10
20	6 × 4	6 × 5	4 × 4	22 × 27	40 × 40	45 × 15
21	0	0		5 × 4	12 × 7	
22	5 × 2	12 × 9	4 × 5	20 × 20	50 × 40	52 × 65
23	6 × 2	20 × 12	6 × 5	25 × 25	50 × 50	60 × 62
24	6 × 3	4 × 4		9 × 4	10 × 12	
25	4 × 4	3 × 3		8 × 8	13 × 11	
26	4 × 1	4 × 4		60 × 60	60 × 60	
27	3 × 5	5 × 4		11 × 11	24 × 20	
28	4 × 4	4 × 4		70 × 30	130 × 75	
29	7 × 5	5 × 2		30 × 26	60 × 40	
30	4 × 2	3 × 5		16 × 19	10 × 11	
31	9 × 13	10 × 11		21 × 20	22 × 21	
32	4 × 2	2 × 5		37 × 45	37 × 25	
33	15 × 18	11 × 9		45 × 70	100 × 50	
34	5 × 5	5 × 4		12 × 15	15 × 10	
35	4 × 3	3 × 1		6 × 6	4 × 3	
36	3 × 1	3 × 1		10 × 6	8 × 5	
37	4 × 3	5 × 3		7 × 6	5 × 5	
38	4 × 2	0		3 × 2	0	
39	20 × 20	6 × 6†		50 × 50	13 × 5†	

* Subjects 19 to 29 inclusive received 0.02 cc. of protamine toxoid (1 to 10 dilution) and 0.1 cc. of "fluid" toxoid (1 to 20 dilution); subjects 30 to 35 inclusive, 0.05 cc. of protamine toxoid (1 to 10) and 0.1 cc. of "fluid" toxoid (1 to 20); subjects 36 to 38 inclusive, 0.05 cc. of protamine toxoid (1 to 10) and 0.05 cc. of "fluid" toxoid (1 to 20). Subject 39, when a Schick test indicated marked sensitivity, was given 0.02 cc. of a 1 to 10 dilution of protamine toxoid and 0.1 cc. of a 1 to 200 dilution of "fluid" toxoid.

† Ninety-six hour reading.

used for immunization were from 3 to 200 times as large as those produced by the protamine toxoid. In those subjects (19 to 29) who received two and one-half times as much "fluid" toxoid as protamine toxoid the areas of erythema were 18 to 600 times as great for the former as for the latter in 8 out of 10 subjects; in the remaining 2 they were about 8 times as great. In the group in which twice as much protamine toxoid as "fluid" toxoid was given 2 subjects

1a. This is a preparation used for performing the so-called "sensitivity" or "reactor" test. The reason that 0.1 cc. of this preparation was injected in most of these subjects is that protamine toxoid was later to be given to them subcutaneously, and the area of erythema produced by the intradermal injection of the standard amount of "fluid" toxoid employed currently in the "reactor" test (0.1 cc. of a 1 to 20 dilution of regular "fluid" toxoid) was to be used as a guide to the volume to be administered subcutaneously. The intradermally injected dose of protamine toxoid was kept in about half the cases at 0.02 cc. of a 1 to 10 dilution in order to learn how the subjects in table 1 might have been expected to react to 0.1 cc. of "fluid" toxoid (1 to 20 dilution), since they also were to receive subcutaneous injections.

1. Subject 16 is omitted from this calculation.

(36 and 37) had respectively twenty and three times as large an area of erythema at the site of injection of the latter preparation as at the site of injection of the former. In the third subject (38) the areas were about the same. Finally, in subject 39 four times as much protamine toxoid as "fluid" toxoid produced only one-sixth as large an area of erythema. The wide variations may be due in part to the fact that reactions are not produced by the same antigen or antigens in all persons. One person may be sensitive to one or more than one component of the toxoid preparation, while a second person may also be sensitive to one or more components, some or all of which may be different from those to which the first subject reacts. In addition, the degree of sensitivity to a given antigen varies in different subjects.

A similar experiment has recently been done in which all three preparations (C.04 cc. of a 1 to 20 dilution of each) were injected intradermally at the same time into 20 adults, the relative sites of injection of the three materials varying from person to person. The protamine toxoid employed in this test was made from the same kind of broth as was used before, but the "fluid" toxoid was made from broth which contained only 75 per cent as much veal extract as was formerly used, and the alum-precipitated toxoid was in turn made from this "fluid" toxoid. Table 3 shows the results. Here also areas of erythema were considerably larger and intensities noticeably greater with the last two preparations.

IMMUNIZING PROPERTIES OF PROTAMINE TOXOID AS DETERMINED IN GUINEA PIGS

A number of experiments have been done over a period of time to test the immunizing capacity of the new preparation. Each experiment was done with a different lot of protamine toxoid, so that the data are both a measure of the efficacy of the material as an immunizing agent and a test of the method of preparing it. One cubic centimeter (25 Lf) of protamine toxoid was injected subcutaneously into guinea pigs, which were bled four weeks later. The serums of 4 or 5 animals were pooled and tested by the Ehrlich method. Twenty-five such preparations were thus tested. Five produced 1 unit of antitoxin per cubic centimeter of guinea pig serum, 6 produced 2 units, 8 produced 3 units (with 3 of these a test for more than 3 units was not done), 4 produced 4 units (with 2 of these a test for more than 4 units was not done) and 2 produced 5 units. In two of the five experiments in which 1 unit of antitoxin was found the Ehrlich test was done with pigs

weighing only 205 to 215 Gm., for lack of animals weighing 250 Gm. A preparation tested on guinea pigs four and one-half months after it had been prepared (during which time it had been kept at room temperature) elicited 3 unit of antitoxin per cubic centimeter of pooled serum showing no detectable loss in antigenicity. It was also effective in converting positive reactions to the Schick test in children to negative reactions. Another preparation, which had been kept in the refrigerator for thirteen months, also was active.

The following data give some information concerning the duration of immunity in guinea pigs. In an experiment in which the initial value (four weeks after an injection of 1 cc. of protamine toxoid) was 3 units of antitoxin there was 1 unit after eleven weeks, the same after fifteen and one-half weeks, 0.5 unit after twenty-five weeks and 0.5 to 1 unit after one year.² In another experiment in which the first value was 3 units there was 2 units after eleven weeks, 1 unit after fifteen and one-half weeks, 0.6 to 0.8 unit after twenty-five weeks, nearly 1 unit after one year² and 0.2 to 0.5 unit after one and one-half years. The pooled serums of a third group of animals which had produced 2 units after four weeks contained less than 1 unit after three months.

The following experiments give additional data regarding the duration of immunity in guinea pigs. They also show the extent of production of antitoxin after a second dose of protamine toxoid. In an experiment in which 1 unit of antitoxin was formed in four weeks 0.7 unit was found after six months. At this time another injection of 1 cc. of toxoid was given. Six weeks later there was at least 7 units of antitoxin per cubic centimeter of pooled serum; tests for more than 7 units were not done. In another experiment in which 1 unit of antitoxin was present at the time of the first test there were 4 units six weeks after a second injection. Two units of antitoxin per cubic centimeter of pooled serum was present after the first injection of toxoid in another instance. After three months there was between 1 and 1½ units, and after six months there was 0.9 unit per cubic centimeter. A second injection was then given, consisting of 0.5 cc. Six weeks later there was at least 7 units of antitoxin per cubic centimeter. Still another group of animals that produced 1 unit of antitoxin after the first injection of protamine toxoid produced 7 units after a second injection.

2. The fact that the values were somewhat higher after a year than after twenty-five weeks may be due to the circumstance that it was not always the same 4 guinea pigs from the group of 6 animals immunized that were bled.

OBSERVATIONS AFTER SUBCUTANEOUS ADMINISTRATION OF PROTAMINE TOXOID TO ADULT HUMAN BEINGS

Each of the subjects listed in tables 1 and 2 subsequently received two or three subcutaneous injections of protamine toxoid. The interval of time between injections was generally three weeks, and the preparations contained 25 Lf units per cubic centimeter. The site of the injection was examined twenty-four, forty-eight and seventy-two hours later and sometimes at intervals thereafter. Measurements were made of the erythema and of the induration.

Results with Subjects Who Had Had the Standard "Sensitivity" Test.—The results obtained with subjects 19 to 35 inclusive, recorded herewith, are of particular interest, since the "sensitivity" ("reactor") test had been done on these subjects in the standard manner. It is generally recommended that if this test produces an area of erythema of 12 by 12 mm. or larger it is inadvisable to inject 1 cc. of "fluid" or alum-precipitated toxoid at one time. The reactions recorded should be compared with the results in table 2. At the end of the description of the observed reactions for each of subjects 19 to 35 inclusive there are given in parentheses the measurements of the erythematous area produced by the "sensitivity" test.

SUBJECT 19.—Erythema 7 by 6 cm. with induration 3 by 3 cm. twenty-four hours after administration of 1 cc. of toxoid. Erythema 15 by 11 cm. with induration 3 by 3 cm. in forty-eight hours. Twenty-four hours after second dose (1 cc.) erythema 8 by 7 cm. with induration of 3 by 3 cm. All gone in forty-eight hours. (40 by 21 mm.)

SUBJECT 20.—Slight erythema 2 by 2 cm. with induration 3 by 3 cm. twenty-four hours after administration of 0.5 cc. After forty-eight hours erythema 3 by 3 cm. with induration 4 by 4 cm. Twenty-four hours after second dose (1 cc.) erythema 9 by 10 cm. with induration 5 by 5 cm. After forty-eight hours erythema 14 by 13 cm. with induration 4 by 3 cm. (40 by 40 mm.)

SUBJECT 21.—Pale erythema 3.5 by 3 cm. with slight induration twenty-four hours after administration of 1 cc. After forty-eight hours pale erythema 3.5 by 3 cm. with slight induration. Twenty-four hours after second dose (1 cc.) moderate erythema 5 by 4.5 cm. with a little induration. After forty-eight hours very pale erythema 6 by 5 cm. with little or no induration. (12 by 7 mm.)

SUBJECT 22.—Erythema 4.5 by 3 cm. with induration 2 by 1 cm. twenty-four hours after administration of 0.25 cc. After forty-eight hours erythema 10 by 11 cm. with induration 4 by 4 cm. After seventy-two hours erythema 10 by 12 cm. with induration 4 by 4 cm. After six days an area 3 by 3 cm. slightly tan and induration 1 by 1 cm. Twenty-four hours after administration of second dose (0.25 cc.) pale erythema 4 by 4 cm. with induration 2 by 2 cm. After forty-eight hours erythema 9 by 12 cm.; no induration. Twenty-four hours after third dose (0.5 cc.) erythema 5 by 6

cm. with no induration. After forty-eight hours very faint erythema 7 by 8 cm. After seventy-two hours all gone. (52 by 65 mm.)

SUBJECT 23.—Erythema 3 by 4 cm. with induration 2 by 3 cm. twenty-four hours after administration of 0.25 cc. After forty-eight hours erythema 8 by 10 cm. with induration 3 by 4 cm. After seventy-two hours moderate erythema 12 by 12 cm. with no induration. After six days all gone; not seen between third and sixth days. Twenty-four hours after second dose (0.5 cc.) erythema 12 by 7 cm. with slight induration 3 by 2 cm. After forty-eight hours erythema 9 by 12 cm. with no induration. Twenty-four hours after third dose (0.5 cc.) pale erythema 5 by 3 cm. with no induration. After forty-eight hours all gone. (60 by 62 mm.)

SUBJECT 24.—Moderate erythema 5.5 by 4 cm. with induration twenty-four hours after administration of 1 cc. After forty-eight hours erythema 9 by 8 cm. with induration 5 by 4 cm. After seventy-two hours erythema 6 by 5.5 cm. with reduced induration. Twenty-four hours after second dose (1 cc.) pale erythema 5 by 4 cm. with induration 2 by 2 cm. After forty-eight hours pale erythema 7 by 6 cm., with little or no induration. (10 by 12 mm.)

SUBJECT 25.—Erythema 3 by 1 cm., with induration 1 by 1 cm. twenty-four hours after administration of 0.5 cc. After forty-eight hours very pale erythema 2.5 by 3.5 cm. with some induration. After four days no erythema; very little induration. Twenty-four hours after second dose (0.5 cc.) erythema 3 by 4 cm. with no induration. After forty-eight hours erythema 6 by 7 cm.; no induration. After six days all gone; not seen between third and sixth days. Forty-eight hours after third dose (1 cc.) moderate erythema 5.5 by 8 cm. Not seen in twenty-four hours or after second day. (13 by 11 mm.)

SUBJECT 26.—Moderate erythema 10 by 8 cm. with no induration twenty-four hours after administration of 0.25 cc. After forty-eight hours erythema 11 by 12 cm. with induration 3 by 3 cm. After six days no erythema; very little induration. Not seen between second and sixth days. (60 by 60 mm.)

SUBJECT 27.—Erythema 3 by 2.5 cm., with induration 2 by 2 cm., twenty-four hours after administration of 0.5 cc. Not seen again till fourth day, when there was erythema with induration 2.5 by 2.5 cm. Twenty-four hours after second dose (1 cc.) erythema 9 by 7 cm. with induration 4 by 3 cm. After forty-eight hours erythema 14 by 13 cm. with induration 4 by 3 cm. (24 by 20 mm.)

SUBJECT 28.—Erythema 4 by 4 cm. with induration 2 by 1 cm. twenty-four hours after administration of 0.25 cc. After forty-eight hours erythema 9 by 10 cm. with induration 2 by 2 cm. After six days no erythema; induration 1 by 1 cm. Not seen between second and sixth days. Twenty-four hours after second dose (0.5 cc.) erythema 7 by 6 cm. with induration 3 by 3 cm. After forty-eight hours erythema 12 by 9 cm. with no induration. Twenty-four hours after third dose (0.5 cc.) mild erythema 7 by 6.5 cm. After forty-eight hours very pale erythema 7 by 6 cm. After seventy-two hours very faint erythema 1.5 by 1 cm. No induration at any time. (130 by 75 mm.)

SUBJECT 29.—Erythema 3 by 3 cm. with induration 1 by 1 cm. twenty-four hours after administration of 0.25 cc. After forty-eight hours erythema 4 by 5 cm. with induration 2 by 2 cm. On sixth day no erythema;

very little or no induration. Not seen between second and sixth days. Twenty-four hours after second dose (0.5 cc.) erythema 4 by 4 cm. with no induration. After forty-eight hours erythema 4 by 4 cm. with no induration. Twenty-four hours after third dose (1 cc.) erythema 6 by 7 cm. After forty-eight hours faint erythema 8 by 6 cm. After seventy-two hours faint erythema 6.5 by 7 cm. No induration at any time. (60 by 40 mm.)

SUBJECT 30.—Very pale erythema 3.5 by 2.5 cm. with little or no induration twenty-four hours after administration of 1 cc. After forty-eight hours erythema 7 by 6 cm. with little induration. Twenty-four hours after second dose (1 cc.) erythema 6 by 4 cm. with induration 2 by 2 cm. After forty-eight hours erythema 5 by 3 cm. with induration 5 by 3 cm. (15 by 19 mm.)

SUBJECT 31.—Erythema 6 by 5 cm. with induration 2 by 2 cm. twenty-four hours after administration of 1 cc. After forty-eight hours erythema 7 by 8 cm. with induration 4 by 4 cm. After seventy-two hours erythema 10 by 10 cm. with induration 4 by 4 cm. Twenty-four hours after second dose (1 cc.) erythema 4.5 by 5 cm. with some induration. (22 by 21 mm.)

SUBJECT 32.—Erythema 4 by 4 cm. with induration 2 by 3 cm. twenty-four hours after administration of 1 cc. After forty-eight hours erythema 8 by 8 cm. with induration 3 by 3 cm. After seventy-two hours erythema 4 by 4 cm. with induration 1 by 1 cm. Twenty-four hours after second dose (1 cc.) mild erythema 9 by 7 cm. with slight induration 2 by 2 cm. After forty-eight hours erythema 9 by 12 cm., hardly visible. (37 by 45 mm.)

SUBJECT 33.—Erythema 4 by 4 cm. with no induration twenty-four hours after administration of 0.25 cc. After seventy-two hours mild erythema 8 by 6 cm. with no induration. On sixth day all gone. Not seen between third and sixth days. Twenty-four hours after second dose (0.5 cc.) erythema 10 by 8 cm. with induration 2 by 2 cm. After forty-eight hours all gone. Twenty-four hours after third dose (0.5 cc.) slight erythema 7 by 6.5 cm. with no induration. After forty-eight hours slight erythema 7 by 6 cm. with no induration. After seventy-two hours all gone. (100 by 50 mm.)

SUBJECT 34.—Erythema 3 by 2 cm. with induration 3 by 2 cm. twenty-four hours after administration of 1 cc. After forty-eight hours erythema 5 by 6 cm. with induration 2 by 2 cm. Twenty-four hours after second dose (1 cc.) erythema 5 by 4 cm. with induration 2 by 2 cm. After forty-eight hours all gone. (15 by 12 mm.)

SUBJECT 35.—Erythema 2 by 1 cm. with induration 2 by 1 cm. twenty-four hours after administration of 1 cc. After forty-eight hours light erythema 5.5 by 3 cm. with very little induration. Twenty-four hours after second dose (1 cc.) very slight erythema 4 by 4 cm. with no induration. (6 by 6 mm.)

Results with Subjects Who Had Received a Modified "Sensitivity" Test.—The following descriptions apply to subjects who had been given intradermal injections of 0.05 cc. each of a 1 to 20 dilution of "fluid" toxoid (one half of the quantity used in the usual "sensitivity" test) as part of an experiment which was done to compare the toxicity of the regular toxoid with that of the new toxoid preparation (see table 2).

SUBJECT 36.—Erythema 2 by 1 cm. with induration 2 by 2 cm. twenty-four hours after administration of 1 cc. After forty-eight hours erythema absent; indura-

tion 4 by 2 cm. Twenty-four hours after second dose (1 cc.) erythema 4 by 4 cm. with no induration. After forty-eight hours erythema 6 by 5 cm. with no induration. After seventy-two hours very pale erythema 5 by 4 cm. with no induration. On sixth day erythema; no induration.

SUBJECT 37.—Erythema 3 by 2 cm. with induration 2 by 1 cm. twenty-four hours after administration of 1 cc. After forty-eight hours erythema 7 by 5 cm. with induration 4 by 4 cm. Twenty-four hours after second dose (1 cc.) pale erythema 4 by 4 cm. with no induration. After forty-eight hours no erythema; no induration.

SUBJECT 38.—Erythema 1 by 1 cm. twenty-four hours after administration of 1 cc. After forty-eight hours no erythema; no induration. Twenty-four hours after second dose (1 cc.) pale erythema 3 by 4 cm. with no induration. After forty-eight hours no erythema; no induration.

SUBJECT 39.—Erythema 5 by 8 cm. with induration 4 by 4 cm. twenty-four hours after administration of 0.25 cc. After forty-eight hours erythema 12 by 1 cm. with induration 5 by 5 cm. After seventy-two hours erythema 15 by 11 cm. with induration 6 by 6 cm. After ninety-six hours erythema 15 by 15 cm. with induration 4 by 4 cm. On sixth day no erythema induration 3 by 3 cm. Twenty-four hours after second dose (0.25 cc.) pale erythema 6 by 5 cm. with slight induration 3 by 3 cm. After forty-eight hours pale erythema 7 by 8 cm. with induration 0.5 by 0.5 cm. Twenty-four hours after third dose (0.5 cc.) erythema by 7 cm. After forty-eight hours erythema 7.5 by 8 cm.

Results with Subjects Who Had Not Received a Standard Sensitivity Test.—It is also of interest to record the reactions observed in those subjects on whom a preliminary sensitivity test as usually done, was not performed. These subjects had been used for a comparison of the relative irritant properties of alum-precipitated toxoid and protamine toxoid by means of intradermal injection of small amounts (see table 1). It is felt that a record of the observations made after subcutaneous injections in these subjects will contribute to a proper estimate of the value of the new preparation.

SUBJECT 1.—Pale erythema 3.5 by 2 cm. with induration 3.5 by 2 cm. twenty-four hours after administration of 0.5 cc. Subject not seen again till fifth day, when erythema and induration were gone. Twenty-four hours after second dose (1 cc.) erythema 6 by 5 cm. with induration 3 by 3 cm.

SUBJECT 2.—Very pale erythema 2 by 1.5 cm. with slight induration, twenty-four hours after administration of 1 cc. After forty-eight hours very pale erythema 2 by 1.5 cm. with slight induration. After seventy-two hours no erythema; slight induration. Twenty-four hours after second injection (1 cc.) erythema 4 by 3 cm. with induration 4 by 5 cm. After forty-eight hours erythema 4 by 4 cm. with induration 1 by 1 cm.

SUBJECT 3.—Very pale erythema 3 by 1 cm. with slight induration twenty-four hours after administration of 1 cc. Subject not seen again till fifth day, when site

3. In the intradermal test this subject received injections of 0.02 cc. of a 1 to 10 dilution of protamine toxoid and 0.1 cc. of a 1 to 200 dilution of "fluid" toxoid.

as normal. Twenty-four hours after second dose of 0.5 cc. erythema 6 by 5 cm. with no induration. After forty-eight hours slight erythema 6 by 5 cm. with no induration.

SUBJECT 4.—Erythema 3 by 2 cm. with slight induration 2 by 2 cm. twenty-four hours after administration of 0.5 cc. After forty-eight hours erythema 4 by 3 cm. with induration 5 by 4 cm. After seventy-two hours erythema 4.5 by 5 cm. with little or no induration. Twenty-four hours after second dose (1 cc.) erythema 4 by 3 cm. with induration 2 by 2 cm. After forty-eight hours slight erythema 7 by 6 cm. with mild induration 3 by 2 cm. On sixth day erythema; induration 3 by 3 cm.

SUBJECT 5.—Erythema 5 by 4 cm. with induration 2 by 2 cm. twenty-four hours after administration of 0.5 cc. After forty-eight hours erythema 7 by 8 cm. with induration 4 by 4 cm. Twenty-four hours after second dose (1 cc.) erythema 10 by 9 cm. with no induration. After seventy-two hours erythema hardly visible.

SUBJECT 6.—Very pale erythema 2.5 by 3 cm. with no induration twenty-four hours after administration of 0.5 cc. After forty-eight hours erythema 5 by 5 cm. After seventy-two hours erythema 6.5 by 8 cm. On fifth day very pale erythema 5 by 7 cm. with no induration. Twenty-four hours after second dose (0.5 cc.) erythema 7 by 5 cm. with little or no induration. After forty-eight hours erythema 8 by 8 cm. After seventy-two hours erythema 9 by 9 cm. with induration 1 by 1 cm. Twenty-four hours after third dose (1 cc.) erythema 9 by 7 cm. with induration 4 by 4 cm. After forty-eight hours erythema 10 by 10 cm. with no induration.

SUBJECT 7.—Erythema 3 by 3 cm. with induration 1 by 3 cm. twenty-four hours after administration of 0.5 cc. After forty-eight hours erythema 8 by 8 cm. with induration 4 by 4 cm. Twenty-four hours after second dose (1 cc.) erythema 6 by 6 cm. with induration 1 by 2 cm. After forty-eight hours pale erythema 10 by 9 cm. with no induration.

SUBJECT 8.—No erythema and no induration twenty-four and forty-eight hours after administration of 0.5 cc. Twenty-four hours after second dose (1 cc.) erythema 1 by 5 cm. with induration 2 by 2 cm.

SUBJECT 9.—Erythema 6 by 4 cm. with induration 2 by 2 cm. twenty-four hours after administration of 1 cc. After forty-eight hours erythema 10 by 7 cm. with no induration. Twenty-four hours after second dose (1 cc.) pale erythema 6 by 7 cm. with no induration. After forty-eight hours pale erythema 10 by 3 cm. with no induration. After seventy-two hours no erythema; slight induration.

SUBJECT 10.—Erythema 5 by 5 cm. with induration 3 by 2 cm. twenty-four hours after administration of 0.5 cc. After seventy-two hours pale erythema 12 by 11 cm. with induration 2 by 2 cm. Twenty-four hours after second dose (0.5 cc.) erythema 4 by 4.5 cm. with no induration. After forty-eight hours erythema 8 by 8.5 cm. with mild induration 2 by 2 cm. Twenty-four hours after third dose (0.5 cc.) erythema 5 by 5.5 cm. After forty-eight hours erythema 4.5 by 5 cm.

SUBJECT 11.—Erythema 5 by 6 cm. with induration 3 by 3 cm. twenty-four hours after administration of 0.25 cc. After forty-eight hours erythema 9 by 12 cm. with no induration. On fifth day no erythema; slight induration. Twenty-four hours after second dose of 0.5 cc. erythema 8 by 9 cm. with no induration. After

forty-eight hours erythema 15 by 12 cm. with little or no induration.

SUBJECT 12.—Very pale erythema 2 by 1.5 cm. with a little induration twenty-four hours after administration of 0.5 cc. After forty-eight hours same. On fifth day all gone. Subject not seen between second and fifth days. Twenty-four hours after second dose of 0.5 cc. erythema 5 by 3 cm. with induration 5 by 3 cm. After forty-eight hours very pale erythema 5 by 6 cm. with induration 3 by 3 cm. Twenty-four hours after third dose of 1 cc. erythema 3.5 by 4 cm. with induration 1 by 1 cm. After forty-eight hours pale erythema 4 by 3 cm.

SUBJECT 13.—Erythema 3 by 3 cm. with induration 3 by 3 cm. twenty-four hours after administration of 0.5 cc. After forty-eight hours erythema 6 by 7 cm. with induration 4 by 4 cm. Twenty-four hours after second dose (1 cc.) pale erythema 7 by 6 cm. with no induration.

SUBJECT 14.—Erythema 4 by 3 cm. with induration 2 by 2 cm. twenty-four hours after administration of 0.25 cc. After forty-eight hours erythema 6 by 7.5 cm. with little induration. After seventy-two hours erythema 9 by 10 cm. with induration 3 by 3 cm. Twenty-four hours after second dose (0.5 cc.) erythema 6 by 5 cm. with mild induration 6 by 7 cm. Twenty-four hours after third dose (0.75 cc.) marked erythema 4.5 by 4.5 cm. with no induration. After forty-eight hours erythema 7.5 by 6 cm. with no induration.

SUBJECT 15.—No erythema or induration twenty-four hours after administration of 0.5 cc. No erythema or induration twenty-four hours and forty-eight hours after second dose (0.5 cc.). Twenty-four hours after third dose (1 cc.) pale erythema 2 by 2 cm. with no induration.

SUBJECT 16.—Erythema 5 by 5 cm. with induration 5 by 5 cm. twenty-four hours after administration of 1 cc. Forty-eight hours after second dose of 1 cc. no erythema or induration.

SUBJECT 17.—Erythema 4.5 by 5 cm. with little or no induration twenty-four hours after administration of 0.5 cc. After forty-eight hours erythema 5.5 by 7 cm. with a little induration. Twenty-four hours after second dose of 1 cc. erythema 8 by 9 cm. with induration 2 by 2 cm. After forty-eight hours very pale erythema 7 by 7 cm. with little or no induration.

SUBJECT 18.—Erythema 4.5 by 4.5 cm. with induration 4.5 by 4.5 cm. twenty-four hours after administration of 1 cc. After forty-eight hours erythema 8 by 9 cm. with induration 6 by 6 cm. Twenty-four hours after a second dose (1 cc.) very pale erythema 3.5 by 3 cm. with little or no induration. After forty-eight hours very pale erythema 7 by 7 cm. with little or no induration.

No systemic reactions were observed in any of these subjects. Slight soreness was reported in a few instances, but in no case was motion of the arm restricted.

Subjects 41, 42, 43, 46, 50, 51, 52, 53, 54, 56 and 59 were recently given subcutaneous injections of 1 cc. (25 Lf units) of protamine toxoid (table 3 shows results of intradermal tests). After twenty-four hours subject 41 had slight erythema 2 by 2 cm., subject 50 very slight erythema 2 by 1 cm., subject 56 moderate erythema 3 by 3 cm. and subject 59 mild erythema 4 by 4 cm. The remaining 7 subjects

had no erythema. Subjects 45 and 57 received 0.25 and 0.50 cc. respectively. An erythematous area measuring 10 by 5 cm. developed next day in subject 45, and he had a temperature of 100.5 F. It will be seen from table 3 that the "sensitivity" test, which was done with 0.04 cc. instead of 0.10 cc. of a 1 to 20 dilution of "fluid" toxoid, produced an erythema of 45 to 60 mm. in this subject. There was a central area of erythema (not recorded in table 3) measuring 16 by 24 mm. and very red. At the site of the intradermal injection of alum-precipitated toxoid (also 0.04 cc. of a 1 to 20 dilution) the erythema measured 55 by 45 mm. and there was a small central necrotic area on the third day. Subject 57 had an erythema of 5 by 4 cm. the day after he received 0.50 cc.

1 cm., after twenty-four hours; after forty-eight hours there was moderate erythema 7.5 by 8 cm with no induration. In the intradermal "sensitivity" test erythema developed 45 by 30 mm and 22 by 22 mm. after the injection of 0.04 cc of alum-precipitated and of "fluid" toxoid respectively. Subject 57, who previously had received 0.5 cc., now received 1 cc. He had induration 2 by 2 cm., with no erythema, after forty eight hours. He was not seen after twenty-four hours. Injections of 0.25 cc. of toxoid were given to subjects 40, 45 (second dose), 49 and 58. Subject 40 had moderate erythema 0.5 by 0.5 cm., with induration 0.5 by 0.5 cm., after twenty-four hours and moderate erythema 3.5 by 2 cm., with the same sized induration, after forty

TABLE 3.—Erythema Produced by Intradermal Injection of 0.04 Cc. of a 1 to 20 Dilution of Protamine Toxoid, Alum-Precipitated Toxoid and "Fluid" Toxoid (Diphtheria) in Adults

Subject	Protamine Toxoid Erythema (in Mm.)			Alum-Precipitated Toxoid Erythema (in Mm.)			"Fluid" Toxoid Erythema (in Mm.)		
	After 24 Hr.	After 48 Hr.	After 72 Hr.	After 24 Hr.	After 48 Hr.	After 72 Hr.	After 24 Hr.	After 48 Hr.	After 72 Hr.
40	10 × 9	23 × 23	14 × 14	26 × 26	47 × 48	35 × 30	18 × 15	40 × 34	32 × 35
41	0	0	0	8 × 7	2 × 2	2 × 2	3 × 2	6 × 6	0
42	2 × 3	0	0	6 × 6	5 × 4	5 × 4	5 × 3	4 × 3	3 × 5
43	5 × 4	5 × 3	5 × 2	12 × 12	7 × 7	7 × 7	5 × 5	5 × 5	6 × 5
44	7 × 10	25 × 20	14 × 12	22 × 22	30 × 38	34 × 35	18 × 18	36 × 38	45 × 40
45	15 × 17	25 × 22	8 × 9	26 × 22	55 × 45	*	35 × 20	45 × 60	*
46	0	0	0	14 × 12	3 × 3	3 × 3	6 × 5	4 × 4	5 × 4
47	20 × 20	†	†	22 × 26	†	†	30 × 30	†	†
48	4 × 3	3 × 3	30 × 20	60 × 35	8 × 9
49	9 × 8	35 × 30	10 × 8	30 × 22	56 × 56	45 × 40	40 × 26	70 × 92	45 × 100
50	4 × 2	2 × 3	11 × 10	2 × 3	8 × 10	5 × 5
51	5 × 3	3 × 2	10 × 12	30 × 20	7 × 7	*
52	3 × 3	0	12 × 10	0	6 × 7	0
53	3 × 2	3 × 1	4 × 5	3 × 3	6 × 5	3 × 6
54	3 × 3	3 × 2	9 × 8	3 × 3	4 × 4	*
55	7 × 6	5 × 6	16 × 20	55 × 30	6 × 10	22 × 22
56	6 × 4	7 × 7	10 × 8
57	10 × 10	22 × 20	11 × 17	35 × 37	15 × 20	25 × 40
58	10 × 17	8 × 12	20 × 22	35 × 45	44 × 22	70 × 55
59	7 × 4	4 × 3	16 × 22	7 × 7	8 × 9	6 × 4

* Limits of erythema are vague.

† Areas of erythema produced by alum-precipitated and "fluid" toxoid became fused and extended into that produced by protamine toxoid.

Six weeks later subjects 41, 46, 50, 51, 52, 53, 54 and 59 again received injections of 1 cc. of protamine toxoid. Subject 41 had very pale erythema, 1 by 1 cm., with no induration, after twenty-four hours, and very pale erythema 2 by 1 cm., with no induration, after forty-eight hours. Subject 50 had slight erythema 2 by 2 cm., with no induration, in twenty-four hours; after forty-eight hours there was neither erythema nor induration. Subject 51 had pale, diffuse erythema 3.5 by 4 cm., with no induration, after twenty-four hours; after forty-eight hours there was neither erythema nor induration. Subject 53 had no erythema nor induration after twenty-four hours; after forty-eight hours there was very pale erythema 2.5 by 3 cm., with no induration. Neither erythema nor induration developed in the remaining subjects after the first or second day. At this time subject 55 received injection of 1 cc. for the first time. He had mild erythema 3.5 by 4.5 cm., with induration 1 by

eight hours. In the "sensitivity" test erythemic areas 47 by 48 mm. and 40 by 34 mm. developed at the sites of injection of alum-precipitated toxoid and of "fluid" toxoid respectively. Subject 45 had moderate erythema 4 by 4 cm., with some induration, after twenty-four hours and pale erythema 3.5 by 2 cm., with no induration, after forty-eight hours. There was no rise in temperature this time. Subject 49 had slight erythema 6.5 by 2 cm., with induration 5.5 by 4 cm., after twenty-four hours, with a rise in temperature to 102 F. Next morning the temperature was normal and there was moderate erythema 10 by 11 cm., with induration 5 by 5 cm. Subject 58 had erythema 8 by 8 mm. and a temperature of 101.8 F. after twenty-four hours. Next morning his temperature was normal. In subject 49 erythema developed, measuring 56 by 55 mm. and 70 by 92 mm, after the "sensitivity" test with the alum-precipitated and "fluid" toxoids (0.04 cc. of a 1 to 20 dilution)

respectively. The areas of erythema in subject 58 were 35 by 45 mm. and 70 by 55 mm. at the corresponding sites.

Schick Tests Before and After Injection of Protamine Toxoid in Adults.—Among the 39 adults listed in tables 1 and 2 whose reactions to the subcutaneous injection of protamine toxoid have been described in the text, 9 originally reacted positively to the Schick test. These were subjects 6, 12, 15, 25, 31, 35, 36, 37 and 38. All 9 reacted negatively to the Schick test after the injections. The time between the last injection of protamine toxoid and the date of the second Schick test was as follows: for subject 6, fifty-five days; for subject 12, sixty-one days; for subject 15, sixty-one days; for subject 25, fifty-six days; for subject 31, fifty-six days; for subject 35, forty-seven days; for subject 36, sixty-one days; for subject 37, sixty-one days, and for subject 38, sixty-one days.

In addition, there were 5 young adults not listed in table 1, 2 or 3 who reacted positively to the Schick test and to whom the protamine toxoid was administered without previous testing of their intradermal sensitivity. Of 2 who each received a single dose of 0.25 cc. subcutaneously 1 reacted negatively after the injection, while the other reacted positively, as before. The quantities injected in the other 3 subjects were, respectively: 0.25 and 0.75 cc.; 0.25, 0.75, 0.50 and 0.50 cc., and 0.25, 0.75 and 1.0 cc. All 3 reacted negatively to the Schick test. The intervals between the injections were a week or ten days, and the time which elapsed between the last dose and the second Schick test was six months. No Schick tests were done on the subjects reported on in table 3. Fourteen more young adults not listed in table 1, 2 or 3 who had not received the Schick test and who were not examined for sensitivity received injections of protamine toxoid as follows: Three received 0.25 and 0.75 cc.; 1 received 0.25, 0.25 and 0.50 cc.; 8 received 0.25, 0.75 and 1.0 cc., and 1 received 0.25, 0.75, 0.50 and 0.50 cc. Areas of erythema and induration in these 14 subjects, as well as in the other 5 subjects listed in this paragraph, were observed but not recorded. The range was similar to those previously described except that there were no instances of very large areas of either erythema or induration. An additional subject who received 0.25 cc. refused to continue because of the erythema and the induration.

IMMUNIZATION OF CHILDREN

To date about 2,600 children, predominantly in the 9 to 12 month age group but including children up to 13 years of age, have received

subcutaneous injections of 1 cc. (25 Lf) of protamine toxoid after an initial Schick test. The reaction consisted of mild to moderate erythema seldom exceeding 2 cm. in diameter and almost always disappearing by the fourth day. There was also a mild degree of induration of the same size, or, more frequently, smaller, which gradually diminished in area until in a large majority of children it was hardly detectable after three weeks. Each of about 750 children have been given two doses of 1 cc. (25 Lf units) each at an interval of one month. The reaction after the second injection resembled that after the first.

Of 238 children⁴ who reacted positively to the original Schick test, all but 8 reacted negatively two and one-half to three months after a single injection of 1 cc. After another injection of 1 cc. the Schick test gave negative results in 7 of these 8 children, while the remaining child reacted negatively after a total of three injections. One hundred and nine children originally reacting positively to the Schick test who each received one dose of 1 cc. subcutaneously were tested six to nine months later. All now reacted negatively.

A group of 28 children whose ages ranged from 8 to 13 years were given 1 cc. of protamine toxoid subcutaneously directly after a sample of blood had been drawn for antitoxin titration. The antitoxin content of the blood before and three and one-half to four months after injection of the toxoid was respectively (in units):⁵

Before	After
1/10 to 1/5	1
1 to 2	5
about 1/10	1
1/2	3
1/25 to 1/10	2
1/10	1/2 to 1
1/25	1
1/25	1/2
1/10 to 1/5	3
1/25	3
1/2	2
1/50	1/25 to 1/10
1/50 to 1/25	1/10
1/25	2
1/50 to 1/25	1/2
1/2 to 1	about 8
1/10	2
1/50	1/2 to 1
1/2	2 to 3
1/100 to 1/50	1/10 to 1/5
1/50 to 1/25	1
1/25 to 1/10	3
1/250 to 1/100	8
2 to 3	10 to 12
1/5 to 1/2	10 to 12
1/2000	1/100
1/250 to 1/100	1/5
1/10	4

These data show that there was a definite rise in antitoxin titer after the injection of prot-

4. Forty-eight per cent of these children were between 9 and 12 months old, 22 per cent were from 1 to 3 years old, 21 per cent were from 3 to 7 years old and 9 per cent were from 7 to 13 years old.

5. Miss Frances Clapp, of Lederle Laboratories, Inc., had these determinations made in her laboratory.

amine toxoid, the actual increase varying from subject to subject, as would be expected. Similar experiments with children possessing no antitoxin at the time of immunization are being carried out.

COMMENT

The considerable number of separate protamine toxoid preparations which have been made and found to be effective immunizing agents in guinea pigs and in children indicates that the method outlined for making the protamine toxoid is dependable. It is always desirable to make sure that there has been no loss of toxoid in the first stage. This was done by adding to the 1 cc. quantities of the supernatant 0.25 cc. of a 25 per cent solution of sodium chloride and graduated quantities of antitoxin according to the Ramon procedure. The same ratio of sodium chloride to toxoid is used in testing with antibacterial serum for the removal of bacillary protein. After precipitation of the protamine toxoid by the addition of three volumes of water and its adsorption on the small amount of alum it is desirable to concentrate a portion of the supernate and perform a flocculation test in order to observe whether there has been any loss of toxoid at this stage.

As an alternate method for preparing the protamine toxoid smaller quantities than the 3.5 mg. per cubic centimeter of toxoid recommended earlier in this paper (about 0.5 mg.) have been added without the simultaneous addition of sodium chloride. This precipitates the bacterial protein and leaves the toxoid in solution. The latter may then be precipitated by the addition of more protamine. Such preliminary treatment with protamine (with or without the addition of sodium chloride) for removal of bacillary protein does not interfere with subsequent precipitation of toxoid by alum in the manner employed for preparing the usual alum-precipitated toxoid. One such alum-precipitated toxoid when injected into guinea pigs (1 cc., 25 Lf units) elicited 4 units of antitoxin per cubic centimeter of pooled serum. No test for larger quantities was made.

The results of the intradermal tests show that protamine toxoid is considerably less irritating than either alum-precipitated or "fluid" toxoid. The measurements recorded in the tables, though revealing this, fail to convey the fact that the site of injection of each of the last two preparations was always significantly redder than the site of injection of the protamine toxoid. In order to counteract the effect of possible differences in sensitivity of the skin in different areas the injection of protamine toxoid was sometimes given above and sometimes below the site of

injection of the preparation with which it was being compared on the inner aspect of the lower part of the arm. Analysis of a number of preparations shows that the ratio of toxoid to total nitrogen is about $7\frac{1}{2}$ times more favorable in the case of protamine toxoid than it is for alum-precipitated toxoid. If the nitrogen derived from the protamine itself is disregarded and only that derived from the broth is considered the ratio is probably 15 times more favorable in the former. This fact accounts for the considerably lesser reactions with protamine-precipitated toxoid than with alum-precipitated toxoid.

The reactions following subcutaneous injection of protamine toxoid into children indicate a more rapid disappearance of the induration than occurs with alum-precipitated toxoid, probably owing to the much lower content of solids. Thus one of the undesirable effects of alum-precipitated toxoid is almost entirely absent when protamine toxoid is used. This does not necessarily mean that the site of the injected protamine toxoid fails to act as a reservoir from which toxoid is slowly liberated over a period of time, a behavior to which the immunizing power of alum-precipitated toxoid is ascribed. The antitoxin titers of the serums of guinea pigs immunized with protamine toxoid, when measured at intervals up to a year and a half, suggest a gradual release of the toxoid. It is also important that a second injection of protamine toxoid results in a sharp rise in the level of antitoxin.

In spite of the good results in guinea pigs and the very high percentage of children whose reaction to the Schick test was converted from positive to negative after a single injection of protamine toxoid, it is felt that children should receive two injections of 1 cc. (25 Lf units) each at an interval of one month. The so-called booster dose after three years should also be administered. Adults should likewise be given 2 cc. Until more data are accumulated to indicate that the precaution is unnecessary, it will perhaps be advisable to perform the "sensitivity" test before injecting 1 cc. as a first dose in adults. For children this is unnecessary.

SUMMARY

A description of a method of preparing protamine toxoid for inoculation against diphtheria has been given.

A single injection of 1 cc. (25 Lf units) in guinea pigs elicits approximately 2 to 3 units of antitoxin per cubic centimeter of pooled serum in four weeks. Titrations at intervals indicate that the animals' serum still contains several tenths of a unit of antitoxin per cubic centimeter of serum after one and one-half years.

Observations made after intradermal injection in human adults of the new preparation and of the currently used alum-precipitated and "fluid" toxoids show that the new toxoid produces much less erythema than either of the others.

The reaction following each of two or three subcutaneous injections in 39 adults of quantities from 0.25 to 1 cc. has been recorded. Nine of these subjects reacted positively to the Schick test before the injection and negatively between forty-seven and sixty-one days after the last dose. Nineteen more adults on whom the "sensitivity" test had not been done each received one or more doses (0.25 to 1 cc.) of protamine toxoid. Of these only 5 had received the Schick test immediately before the injection. When these 5 were retested after the injections of protamine toxoid, 4 reacted negatively; the fifth, who had received only 0.25 cc. of toxoid, again reacted positively.

No systemic reaction occurred in any of these subjects. Local reactions consisted of erythema and induration; in no case was the reaction sufficient to restrict motion of the arm, in spite of the fact that 15 of 21 subjects (table 2) had areas of erythema greater than 12 by 12 mm. in response to the "sensitivity" test and that all but 1 in a group of 18 who received 0.02 cc. of a 1 to 10 dilution of alum-precipitated toxoid intradermally also had areas larger than this.

Recently we have encountered, in a new group of 17 adults, 13 of whom had extremely mild reactions to 1 cc., 3 subjects whose temperatures rose to 100.5, 101.8 and 102 F. twenty-four hours after a first injection of 0.25 cc. The next morning the temperatures of the last 2 subjects were normal; that of the first was not taken. A second injection of 0.25 cc. six weeks later produced no rise of temperature in this subject. A "sensitivity" test in which only 40 per cent of the standard amount of "fluid" toxoid and an equivalent amount of alum-precipitated toxoid were injected had indicated that all 3 subjects were extremely sensitive.

In approximately 2,600 children between the ages of 9 months and 13 years (the majority were between 9 and 12 months old) each of whom received 1 cc. of protamine toxoid subcutaneously, only a little erythema and induration were observed. None gave evidence of a systemic reaction, nor did sterile abscesses develop in any. All of these children had received the Schick test before the injection of toxoid. Two hundred and thirty-eight have since been tested after an interval of two and one-half to three months, and 230 of the retests gave negative results. Of the 8 children who still reacted positively, 7 reacted negatively three

months after a second dose, while 1 required three doses before reacting negatively. One hundred and nine children who originally reacted positively to the Schick test reacted negatively six to nine months after a single injection of 1 cc. (25 Lf units). About 750 children have received a second injection of protamine toxoid. The reaction was the same as after the first dose.

After the injection of 1 cc. of protamine toxoid in each of 28 children, all of whom had some antitoxin at the time, a sharp rise in antitoxin occurred when this was measured four and one-half months after the injection.

Lederle Laboratories, Inc., Pearl River, N. Y. (Dr. W. G. Malcolm, director) gave financial aid in this work. Physicians of the New York City Health Department, especially Dr. Bluma Lipshitz, assisted in the immunization of the children.

ABSTRACT OF DISCUSSION

DR. ERNEST L. STEBBINS, New York: It is a pleasure to have the opportunity to discuss Dr. Ross's paper and to comment on the prospects for the development of a new antigen for immunization against diphtheria. Fifteen years ago physicians felt that they had a satisfactory knowledge of diphtheria and of the means of treatment and of prevention. The very fact that during the past fifteen years there has been a rapid development of new antigens for immunization against that disease proves clearly, I think, that the ideal antigen has not as yet been discovered.

There has been fairly general agreement that use of alum-precipitated toxoid is definitely the method of choice of immunization. There is little criticism as to the percentage of persons treated that are rendered immune as measured both by antitoxin titration methods and by actual experience with exposure to the disease. There are certain disadvantages in the use of alum-precipitated toxoid, however. Its restriction to younger children is a minor limitation on its use, but definitely a limitation. There are occasions when immunization of older children and of adults is desirable, and the reaction to the alum-precipitated toxoid interferes with the use of this antigen for that purpose. Then, too, even in younger children the persistent nodule and the rare occurrence of abscess are a disadvantage. Because of the limited number of persons treated and later subjected to antitoxin titrations, the results, while suggestive of definite value, are not, in my opinion, entirely conclusive. A considerable number of the experiments in which titration was done before immunization and after immunization showed that the subjects had had antitoxin before the administration of protamine toxoid.

If subsequent experience indicates that persons with little or no antitoxin prior to immunization show an equally prompt and satisfactory response to the immunizing treatment, there will be much more ground for a change of opinion as to the most desirable agent to use. The evidence seems to be conclusive that the protamine toxoid does produce less serious local and systemic reaction both in older children and adults and in younger children. This is a distinct advantage, and if the potency of the antigen and the production of immunity as measured by antitoxin titration are satisfactory and if the duration of the immunity is comparable to that of the immunity produced by alum-precipitated toxoid, this should mean a definite advance in the means of immunizing against diphtheria.

CONGENITAL ANOMALIES OF THE LOWER PART OF THE RECTUM

ANALYSIS OF SIXTEEN CASES

MADISON J. LEE JR., M.D.

MADISON, WIS.

Congenital anal and rectal malformations are uncommon, occurring in but 1 of about 5,000 infants.¹ There are many reports of these conditions, but only since 1934, when Ladd and Gross published their classification,² has a logical and practical consideration of the subject been feasible. It has been my privilege to review and study the cases of 16 patients with anomalies of this type who were admitted to three hospitals in New Orleans (Charity Hospital, Touro Infirmary and Southern Baptist Hospital) during the past four years.

EMBRYOLOGY AND PATHOGENESIS

A study of the normal development of this region is necessary in order to understand the pathogenesis of malformations of the anus and rectum.

In the embryo of 5 weeks the portion of the urogenital sinus that is to form the trigone of the bladder is continuous, below the point at which it receives the Wolffian ducts, with the cloaca, a terminal cavity common to the urogenital and intestinal tracts. The cloaca is narrow, laterally compressed and closed caudally by the seamlike cloacal membrane. The intestinal tube extends beyond the cloaca toward the tail as the minute caudal intestine. In each lateral wall of the cloaca there is an external longitudinal groove, with a corresponding internal ridge. By the obliteration of the intervening space, the genitourinary and intestinal portions of the cloaca are later differentiated.

In the embryo of 6 weeks further progress toward separation of the urogenital sinus and the intestine is seen. Separation takes place in two ways. By downgrowth of the urorectal septum (a saddle-like strip of mesoderm) the opening between the two systems may be reduced to a

small cloacal duct. Separation may be accomplished also by coalescence of the lateral walls along the longitudinal grooves, allowing mesenchyme to grow across the cloaca. Since the mesenchymal bridge may appear from different parts of the longitudinal groove, variations in the level of the cloacal duct result. If mesenchyme grows across the cloaca at several levels, there may be intervening gaps through which the rectum and the urogenital sinus communicate. Normally, the process of separation obliterates all such communications by the seventh week.

Late in the seventh week a primary perineum is established by division of the cloacal membrane into an anterior urogenital membrane and a posterior anal membrane and by downgrowth and spreading of the mesenchymal elements between these. At the same time the urogenital sinus acquires an external opening, although the anal membrane does not rupture until later. In-pocketing of the anal pit occurs, forming the proctodeum, and continues until the lumens of the proctodeum and the rectum are joined by rupture of the anal membrane. There is some variation, but this rupture usually takes place during the eighth week.

In young embryos the rectal tube appears as a spindle-shaped swelling that persists in modified form until birth. An upper enlargement, the bulbus analis, has a position corresponding closely to that of the adult rectal ampulla. Its walls become invaginated to form longitudinal folds and ridges, the rectal columns. Caudally there is a second swelling, much shorter and less well differentiated, the bulbus terminalis. This swelling is distinct for only a short time, and the region develops into the zona intermedia.

Many rectal and anal malformations may be due to arrests or abnormalities of development during the seventh or eighth embryonic week. Anomalous connections between the rectum and the genitourinary apparatus occur if the cloacal duct fails to close. Rectoperineal fistulas are probably formed by obliteration of the anterior or ventral portion of the cloacal duct with persistence of the dorsal portion; dissolution of the cloacal membrane then results in an external perineal opening.

From the Department of Pediatrics, Tulane University of Louisiana School of Medicine, New Orleans.

1. David, V. C.: Embryology and Malformations of the Rectum, in Nelson Loose Leaf Surgery, New York, Thos. Nelson & Sons, vol. 5, p. 161.

2. Ladd, W. E., and Gross, R. E.: Congenital Malformations of the Anus and Rectum, *Am. J. Surg.* 23:167, 1934.

In a female fetus connections between the rectum and the genital tract are undoubtedly formed during the descent of the region of attachment of the müllerian ducts to the posterior wall of the urogenital sinus; the ducts assume any fistulas already existing between the rectum and the urogenital sinus. Such fistulas may connect the rectum with the vagina or the uterus, commonly the former.

Congenital stenosis may occur at the anus or 1 to 4 cm. higher. Partial obstruction at the anal site results from incomplete rupture of the membrane, and a membranous imperforate anus results from persistence of the anal membrane. Rectal stenosis may result from incomplete development of either the bulbus analis or the bulbus terminalis. In abnormalities in which the rectum ends blindly at a considerable distance above the imperforate anus, the embryonic origin is not clear. Possibly the obliterative process that normally occludes the tailgut may abnormally involve the posterior part of the cloaca and thereby be responsible for such a condition. When the anus and the anal pouch are normal but the rectum ends blindly, it is probable that obliteration occurred at the upper bulbus analis.

It should be pointed out that the presence of the external anal sphincteric muscle is not dependent on the presence of the terminal portion of the bowel, as the muscle develops from the regional mesenchyme. Hence, the external sphincteric muscle may be present with any malformations described here.

TYPES OF MALFORMATIONS

Many classifications have been advanced to cover the various rectal malformations. Bodenbauer,³ in 1860, was the first to make a systematic classification of anomalies of the rectum. Ball⁴ in 1887, Keith⁵ in 1908, Fraser⁶ in 1926, Fitchet⁷ in 1926 and Crowell and Dulin⁸ in 1940 published classifications. However, the most logical and practical grouping is the following, suggested ten years ago by Ladd and Gross²:

3. Bodenbauer, W.: *A Practical Treatise on the Etiology, Pathology and Treatment of the Congenital Malformations of the Rectum and Anus*, New York, S. S. & W. Wood, 1860.

4. Ball, C.: *The Rectum and Anus*, London, Cassell & Co., 1887.

5. Keith, A.: *Malformations of the Hind End of the Body*, Brit. M. J. 2:1736, 1908.

6. Fraser, J.: *Surgery of Childhood*, New York, William Wood & Company, 1926, vol. 2.

7. Fitchet, S. M.: *Imperforate Anus*, Boston M. & S. J. 195:25, 1926.

8. Crowell, E. A., and Dulin, J. W.: *Congenital Anomalies of the Anus and Rectum*, Surgery 7:529, 1940.

Type 1. Incomplete rupture of the anal membrane or stenosis at a point 1 to 4 cm. above the anus.

Type 2. Imperforate anus due to a persistent anal membrane.

Type 3. Imperforate anus with the rectal pouch separated from the anal membrane. The rectal pouch is a closed sac.

Type 4. Normal anus and anal pouch with a blind rectal pouch. There is either membranous obstruction or considerable separation between the two pouches.

Of 16 patients studied recently, 4 (25 per cent) had anomalies of type 1. Two of the 4 had incomplete rupture of the anal membrane, and 2 had congenital stenosis of the anus and the lower part of the rectum.

No simple type 2 malformations were recorded at the three hospitals during the period of this study. Perhaps they occurred, but were treated so easily and satisfactorily by the obvious expedient of simply rupturing the membrane that neonatal stay in the hospital was not extended beyond the usual period and no further medical interest was aroused.

Eleven patients (68.7 per cent) had type 3 malformations. In this as in other series, anomalies of this type are the most common by far.

The remaining patient seems best considered as having anomalies combining types 1, 2 and 4. There were an imperforate anal membrane, stenosis of the anal canal and a normal rectum separated from the sigmoid flexure by a membrane.

SYMPTOMS AND PHYSICAL SIGNS

Since all rectal anomalies except those of type 1 produce intestinal obstruction from birth, they are usually recognized in the first few hours or days. Rarely, the only complaints are those referable to obstruction, such as refusal to nurse, persistent vomiting or abdominal distention. More often, some one notes that there is no anal opening, that no meconium is passed or that it comes from an abnormal exit, such as the vagina, the urethra or a perineal fistula. The abnormality may even be overlooked until, on the second or third day, unsuccessful attempts are made to take the rectal temperature or give an enema. Here it should be emphasized that physical examination of all infants should always be carried out shortly after birth, in order to make an early diagnosis of these and other equally obvious conditions. In infants older than 24 or 48 hours complete occlusion produces features of obstruction of the lower part of the bowel, such as abdominal distention, vomiting,

borborygmus, increased irritability and dehydration, with eventual circulatory or respiratory collapse. For patients with a simple bulging, discolored anal membrane (type 2), the diagnosis is obvious and the treatment is usually completed at once. In patients with anal stenosis or large associated fistulas, the signs of intestinal obstruction may be less evident or may even be missed completely. The perineum often bulges downward when the child strains to defecate, and a ribbon-like stool may be noted.

ROENTGEN FINDINGS

In 1930 Wangenstein and Rice⁹ published a description of a method of determining the position of the blind rectal pouch in patients with imperforate anus. The infant is inverted, and a flat roentgenogram of the abdomen and pelvis is taken, with an opaque marker in the anal dimple or at its usual site. Gas in the intestine rises and outlines the rectal pouch, giving an indication of its position with relation to the external surface of the perineum and the marker. However, this technic has limited value during the first twenty hours of life, because gas has not yet proceeded far enough in most instances to give good visualization.

Roentgen examination is useful in another way. Prior to a plastic perineal operation on patients for whom a defunctionalizing colostomy has previously been performed, barium sulfate or iodized oil can be injected into the distal loop of the intestine to facilitate accurate localization. This procedure, of course, also aids in tracing fistulous communications, especially when combined with fluoroscopic examination.

Berman¹⁰ recommends the use of the fluoroscope as an aid in diagnosis, especially for infants during the first twenty-four hours after birth. By moving the infant into various positions and by gentle massage of the abdomen gas may be forced into the blind pouch of the rectum. The position is then determined in relation to bony landmarks or is marked by metal arrows fastened to the skin with adhesive tape.

ASSOCIATED ANOMALIES

The anomaly most commonly associated with congenital malformations of the anus and rectum is fistula. The types of fistula commonly found in male infants are (1) rectovesical, (2) rectourethral and (3) rectoperineal. In female infants (1) rectovaginal fistulas, (2) rectovesical

fistulas, (3) fistulas between the rectum and the fossa navicularis and (4) rectoperineal fistulas are associated with rectal anomalies.

Eleven of the 16 patients in this series (68.7 per cent) had fistulas. None of the patients with rectal anomalies of type 1 had fistulas, but 10 of the 11 with type 3 anomalies had an associated fistula, as did the patient with "mixed" anomalies. Six had rectovesical fistulas; 3 had rectourethral fistulas, and 2 had rectovaginal fistulas.

Of Berman's¹⁰ 23 patients, 13 (56.5 per cent) had associated anomalies other than fistula. Four had multiple (two to four) anomalies; the others had single anomalies. Ladd and Gross reported 162 cases, in 43 (26.0 per cent) of which there were other anomalies, in some as many as eight. In 12 cases the associated anomaly was the cause of death.

Eleven patients (68.7 per cent) of the group studied here presented associated anomalies other than fistulas. Defects which occurred are listed in the accompanying table. Four of the 11 patients had single anomalies, while 7 had two to five. Only 2 of the 4 patients with type 1 rectal anomaly had other abnormalities, and in each the single malformation was minor. The incidence was much higher in patients with type 3 rectal abnormalities; 8 of 11 had one or more additional defects. The patient with "mixed" rectal anomalies presented multiple associated defects as well, the fistula between the lower part of the rectum and the neural canal being one of the most unusual.

TREATMENT

The treatment of rectal and anal malformations varies with the type of anomaly and the age of the child. It is not the purpose of this paper to describe the various surgical techniques employed. For this the reader is referred to articles by Ladd and Gross,² Crowell and Dulin,⁸ Harken¹¹ and Berman.¹⁰ It can be stated dogmatically that all treatment depends on accurate diagnosis.

Type 1. In the treatment of anomalies of type 1 repeated dilation of the stricture with dilators of various types or with a finger usually suffices to overcome the obstruction. Treatment should be continued for several weeks or months, as necessary. When the opening in the anal membrane is small, obstruction may be relieved by a cruciate incision followed by dilation.

Type 2. Simple cruciate incision of the membrane followed by regular dilation is all that is

9. Wangenstein, O. H., and Rice, C. O.: Imperforate Anus, *Ann. Surg.* **92**:77, 1930.

10. Berman, J. K.: Congenital Anomalies of the Rectum and Anus, *Surg., Gynec. & Obst.* **66**:11, 1938.

11. Harken, D. E.: Congenital Malformations of the Rectum and Anus, *Surgery* **11**:422, 1942.

necessary in the treatment of rectal abnormalities of type 2.

Type 3. The treatment of type 3 abnormalities depends on the position of the rectal pouch. Immediate mobilization of the rectal pouch and proctostomy by the direct perineal approach is the method of choice if the pouch is readily accessible. If it cannot readily be reached in this manner, a colostomy in the transverse colon should be made and plastic repair of the perineal region performed after three or four years.

Careful training helps to overcome this condition. Wreden¹² and Stone¹³ have suggested a plastic operation for this distressing complication.

Another complication which may follow surgical treatment of malformations of the anus and rectum is cicatricial anal stenosis. Cole and Greeley¹⁴ have suggested utilization of pedicle skin grafts in the correction of such a complication.

Three of the 4 patients with type 1 anomalies received dilation, with good results for 2

Data for Sixteen Cases of Congenital Rectal Anomaly

Type of anomaly (according to Ladd and Gross ²).....	I				III										I, II, IV		Total
Case number.....	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
Sex of patient																	
Male.....	+	+	..	+	+	+	..	+	..	+	+	..	+	+	+	+	12
Female.....	+	+	..	+	+	4
Race of patient																	
White.....	..	+	..	+	+	+	..	+	+	+	+	+	+	+	+	+	13
Negro.....	+	..	+	+	3
Fistula																	
Rectovesical.....	+	..	+	+	+	..	+	+	..	6
Rectourethral.....	+	+	+	3
Rectovaginal.....	+	..	+	2
Between rectum and neural canal.....	+	1
Other associated anomalies																	
Sacrocoxygeal dimple.....	+	+	+	..	3
Aural deformity.....	..	+	+	2
Umbilical hernia.....	+	..	+	2
Spina bifida.....	+	+	2
Enlarged heart.....	+	+	2
Anomaly of sacrum.....	+	+	..	2
Imperforate urethra.....	+	1
Dextrocardia.....	+	1
Hermaphroditism.....	+	1
Anomaly of ribs.....	+	1
Malformed vertebrae.....	+	1
Atelectasis of left lung.....	+	1
Undescended testis.....	+	1
Unclassified heart condition.....	+	1
Absence of vagina.....	+	1
Stenosis of colon.....	+	1
Bilateral five fingers, no thumbs.....	+	1
Hydrocele.....	+	1
Total recognized associated anomalies.....	0	1	0	1	1	4	3	0	0	5	2	3	1	0	2	2	25
Treatment																	
Immediate perineal plastic operation.....	+	..	+	++	..	+	..	+	5
Colostomy.....	+	+	+	..	+	+	+	6
Dilation.....	+	+	+	+	4
Lateral perineal plastic operation.....	+	1
Fistula closed later.....	+	1
No specific therapy.....	+	+	2
Present status																	
Good anal function.....	+	+	+	..	+	+	5
Fair anal function.....	+	+	+	3
Patient well, but plastic work to be done.....	+	+	..	+	3
Died from an associated anomaly.....	+	+	+	+	4
Died from the anal anomaly.....	+	1
Died from unrelated cause.....	+	1

Type 4. Anomalies of the fourth type are the most difficult to treat because the rectal pouch is frequently so high in the pelvis that it is hard to reach by the perineal approach. Preliminary colostomy is often necessary. If the obstruction is membranous, incision and dilation from below may suffice.

If fistulas are present, they are usually best left undisturbed during infancy.

Unfortunately, anal incontinence of varying degree follows reconstruction in some instances.

and fair results for 1 of them. The fourth patient left without receiving specific therapy.

Five patients with type 3 anomalies had immediate perineal plastic operations. Two of them

12. Wreden, R. R.: A Method of Reconstructing a Voluntary Sphincter Ani, *Arch. Surg.* **18**:841 (March) 1929.

13. Stone, H. B.: Plastic Operation for Anal Incontinence, *Arch. Surg.* **18**:845 (March) 1929.

14. Cole, W. H., and Greeley, P. W.: Utilization of Pedicle Skin Grafts in Correction of Cicatricial Anal Stenosis, *Surgery* **12**:349, 1942.

can be considered completely normal, now having good anal function. One died shortly post-operatively, and 1 died later of an unassociated cause. The fifth patient has good anal function, but an associated fistula remains to be closed.

Of 4 patients with type 3 anomalies who had colostomies soon after birth, 1 has had two subsequent perineal plastic operations and has fair anal function at present. One died later from an infection of the urinary tract. The other 2 await future plastic perineal repair.

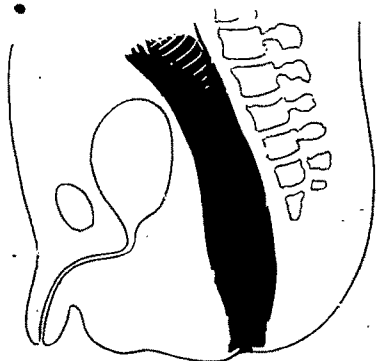


Fig. 1.—Diagram of the condition in case 1; rectal anomaly of type 1, with incomplete rupture of the anal membrane.

One patient with a type 3 malformation died of associated anomalies; the remaining patient in this group was treated by dilation of the opening of a cloaca-like cavity and died after leaving the hospital before treatment had been completed.

The patient with "mixed" anomalies presented a hopeless condition from birth because of multiple anomalies. He died after a palliative cecostomy.

To summarize the results, 6 of 16 patients died. The results were good or fair in all patients with type 1 anomalies who were treated. Of 6 patients with type 3 anomalies who are living, treatment has been completed for 3, with good results in 2 and fair anal function in the third. The other 3 still need further plastic perineal repair.

REPORT OF CASES

Anomalies of Type 1

CASE 1.—A Negro boy 18 months old was admitted to Charity Hospital of New Orleans in November 1941, because of painful, difficult defecation. His appetite had always been good, and he had "never been sick." Physical examination revealed no abnormalities except a small elliptic anus partially occluded by a diaphragm-like margin. Roentgenograms taken after the child had been given an enema of barium sulfate showed no filling defect or deformity of the colon or rectum. After examination and dilation, the patient was discharged from the hospital and had no difficulty for six weeks, when pain and tenesmus recurred. He was then re-

admitted, and the anal slit was found to be too small to admit the tip of a little finger. Simple digital dilation was repeated, and the patient has defecated regularly without difficulty ever since.

CASE 2.—B. L., a white boy born in Touro Infirmary in March 1942, had an almost imperforate anus and a deformity of the right ear which were noted at birth. Roentgen examination of the inverted baby seven and forty-eight hours after birth showed diffuse distention of the gastrointestinal tract to a point 2.2 cm. from a marker at the anal dimple. However further studies made after the introduction of contrast material through the tiny anal orifice indicated that the obstruction was incomplete, probably consisting of a diaphragm-like membrane with a small central aperture. After daily dilation of the rectum with catheters the distention was controlled, and the patient had no further difficulty. He was discharged with instruction for continued dilations at home. No follow-up observations could be secured.

CASE 3.—B. C., a 3 year old Negro girl, was admitted to Charity Hospital of New Orleans in June 1942, because she had been unable to defecate during the last month. Since birth intestinal evacuation had been difficult; enemas had been used at least weekly during the child's entire life. Her appetite had been good, and there was no vomiting. She was well developed and fairly well nourished and presented the classic signs of megacolon. The anus was too small to admit the little finger. After digital dilation and cleansing enemas, intestinal elimination was regular; though occasional enemas are still necessary, the child no longer has unusual enlargement of the abdomen or other features of megacolon.

CASE 4.—K. S., a 16 month old white boy, was admitted to Touro Infirmary in January 1943, with a complaint of "constipation." At birth he had had almost complete anal atresia. Since that time he had had "ribbon stools" once weekly, and frequent enemas had been necessary. At the age of 9 months he had had an

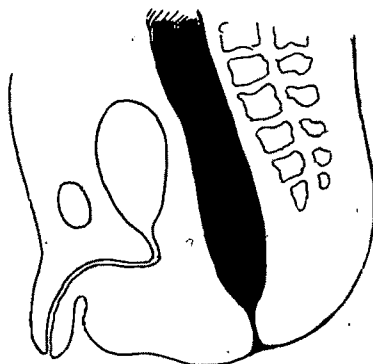


Fig. 2.—Diagram of the condition in case 3; rectal anomaly of type 1, with congenital anal stenosis.

operation to enlarge the anal orifice at another hospital, but this gave no relief. He cried during defecation; his abdomen was protuberant, and abdominal examination showed the classic features of well developed megacolon, together with a large umbilical hernia. The anal orifice would barely admit the tip of a little finger, and fecal impaction was present. He was removed from the hospital the following day without treatment, and no follow-up observations could be secured.

Anomalies of Type 3

CASE 5.—D. B., a 4 year old white boy, was admitted to Charity Hospital of New Orleans in September 1942. At birth an imperforate anus had been noted, and a colostomy was done the next day. The artificial opening had functioned well. At the time he was admitted, the colostomy opening was evident in the right upper quadrant. Anal and sacrococcygeal dimples were present. A week later a perineal dissection was carried 5 inches (12.5 cm.) deep. The blind rectal pouch was identified, mobilized, brought down and sutured to the margin of the skin. After a second

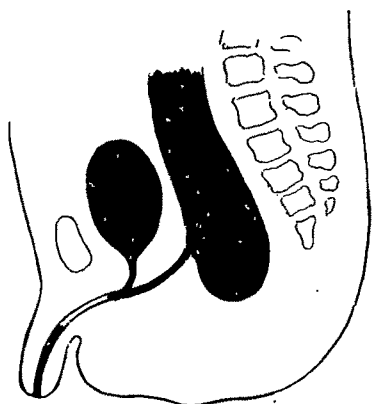


Fig. 3.—Diagram of the condition in case 6; rectal anomaly of type 3, with a rectourethral fistula and an imperforate urethra.

perineal plastic operation, performed two months later, the rectal pouch was opened, and five months later the colostomy was closed. Subsequent dilation has been necessary, and careful training is gradually correcting the patient's moderate anal incontinence.

CASE 6.—E. S., a white boy of 2 days, was admitted to Charity Hospital of New Orleans in October 1941, when absence of the anus was first noted. Physical examination showed a well developed infant who was jaundiced, cried a great deal and had severe abdominal distention. An anal dimple was present. Roentgen observation with the infant inverted showed the gas-filled rectal pouch to be 3 cm. from the dimple. By perineal dissection the rectal pouch was identified, mobilized, brought down, sutured to the margin of the skin and opened. No fistula was found, but a small anterior pouch was tied and cut. Pyelograms made later failed to show a communication between the rectum and the urinary tract, though the child voided through the incision from the beginning, never through the urethra. When the infant was readmitted to the hospital a year later, his development had been normal. His appetite had been good, but he had had constipation and tenesmus. His anus was dilated to the size of an adult middle finger. A small umbilical hernia was present; he had a sacrococcygeal dimple, and roentgen examination revealed spina bifida. Pyelograms and proctoscopy demonstrated a rectourethral fistula and a rectal polyp. When he was circumcised, an unsuccessful attempt was made to pass a filiform catheter into the bladder. Later, suprapubic cystostomy was done. Perineal exploration revealed imperforation of the bulbar portion of the urethra for 1 cm. The continuity of the lumen was reestablished over a catheter, and the rectourethral sinus was ligated. Anal and urethral function continue to be good.

CASE 7.—J. M., a Negro girl, was born in Charity Hospital of New Orleans in November 1941. Physical examination revealed deformities of both ears, imperforate anus and rectovaginal fistula. Her general condition was poor. Roentgen examination revealed enlargement of the heart, dextrocardia, passive congestion of both lungs and enlargement of the liver. Defecation through the vagina was normal. After symptomatic treatment for two weeks, she was discharged from the hospital. When she was readmitted later, the child presented a feeding problem and defecation through the rectovaginal fistula was irregular. No operative procedure was undertaken. The patient became progressively worse and died after nine weeks.

CASE 8.—R. T., a white boy 2 days old, was brought to Charity Hospital of New Orleans in May 1942, when it was noted that there had been no intestinal elimination, that the baby cried excessively, that he was distended and that there was no anal opening. There had been no vomiting. Physical examination revealed absence of an anus or anal dimple; no other abnormalities were noted. Roentgenograms of the inverted infant showed a blind rectal pouch well above the levator muscles. Catheterization showed no meconium in the urine. The rectal pouch was located by perineal dissection at a depth of 3 cm.; it was mobilized, brought down, sutured to the margin of the skin and opened. The child was asymptomatic when he was discharged from the hospital three weeks later. Prior to the readmission of the patient one month later, the stools became much smaller, and tenesmus was obvious. Examination showed a malnourished, anemic infant with a distended abdomen. Feces and urine were passed from the urethra as well as through the small, tight anal opening. Dilation of the rectum with catheters daily for two weeks produced complete relief of symptoms and diminution of fecal admixture in the urine. Occasional dilation was continued at home, and the child has had good anal function ever since. The rectovesical fistula is to be corrected when he is older.

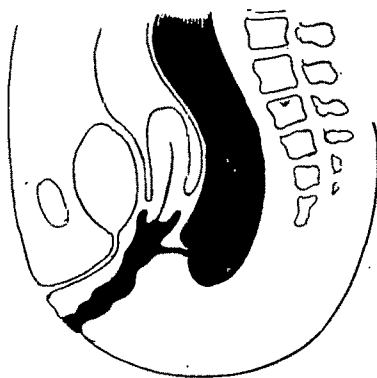


Fig. 4.—Diagram of the condition in case 9; rectal anomaly of type 3, with a rectovesical fistula.

CASE 9.—W. B., a white girl 3 weeks old, was admitted to Southern Baptist Hospital in September 1943. There was no anus or anal dimple. A rectovaginal fistula was present, through which the infant had defecated since birth; there were no signs of intestinal obstruction. By the perineal approach the rectum was located, mobilized, brought down, sutured to the margin of the skin and opened. Another perineal plastic operation was performed a month later, when it was found that the rectum had retracted and the perineum had healed over. Stools were still passed through the vagina, but the child now presented signs of partial

obstruction. Because the perineum again began to heal over, a colostomy was performed. The fistula functioned well. Six weeks later meningitis developed, and the infant died one day after readmission to the hospital. Autopsy showed a well functioning colostomy opening; the perineum was closed over, and a recto-vaginal fistula opened into the upper third of the vagina. No other anomalies were present. The diagnosis of pneumococcal meningitis was confirmed bacteriologically.

CASE 10.—H. C., a white boy 8 hours old, was admitted to Charity Hospital of New Orleans in July 1940. The scrotum was well developed on the right side and contained a normal-sized testicle; the left side of the scrotum was rudimentary, resembling a labial fold, and contained no testicle. The penis was small and anomalous in appearance. One and five-tenths centimeters posterior to the penis was a pinpoint opening from which meconium and urine were extruded; there was no anus or anal dimple. Mechanical dilation was carried out daily until the aperture was 1 cm. in diameter. Both urine and feces were passed through this common opening almost continuously, and there seemed to be no sphincter action. Roentgen examination of the chest showed bizarre irregularities of the ribs, hemivertebrae, absence of vertebrae, enlargement of the cardiac shadow and partial atelectasis of the left lung. Unexplained alternating severe diarrhea and constipation developed, which did not respond to symptomatic measures. The infant died when he was 3 months old. An autopsy was not done.

CASE 11.—R. P., a white boy, was born in Charity Hospital of New Orleans in September 1942. At routine examination an imperforate anus was found. There was also a rough systolic murmur over the entire precordium; the left testicle was undescended, and meconium passed through the urethra with urine. Roentgen examination of the inverted infant at the age of 6 hours showed the gas-filled rectal pouch 2 cm. from the marker. The pouch was located by perineal dissection, freed, pulled down, sutured to the skin and opened. A week later the pouch had to be resutured to the edges of the skin, and there was secondary maceration with infection of the surrounding skin, which healed slowly. After two months in the hospital, the infant was discharged, only to be readmitted six weeks later because of progressive constipation. Formed stools were passed infrequently and with extreme pain. There had been no vomiting; the appetite was excellent, and the gain in weight was adequate. A stricture was found just inside the anal opening, and it was gradually dilated. Now, though frequent dilation is still necessary, the infant appears well and has regular habits of defecation. The action of the anal sphincter appears to be normal.

CASE 12.—J. B., a white girl, was admitted to Touro Infirmary shortly after birth, in August 1943. Physical examination showed absence of the anus or anal dimple, well formed labia, complete absence of the vaginal orifice and enlargement of the clitoris and urethra. Meconium passed through the urethra. Early roentgenograms were not diagnostic, though it appeared that the rectal pouch was separated from the expected anal site by about 6 cm. The right transverse processes of the second and third sacral vertebrae were not visualized. The following day a Devine colostomy was made in the transverse colon. The postoperative course was slow, with difficulty in feeding and maceration of the skin adjacent to the colostomy opening. Studies with diodrast as the contrast medium showed irregularity in the contour of the bladder. The dye entered the in-

testine. No further attempt was made to localize the fistula, and for two months the baby progressed normally. She was then readmitted because of an infection in the upper respiratory tract. Straining and coughing had caused herniation of the distal intestinal loop onto the anterior abdominal wall at the site of the colostomy. The distal loop was easily reduced. After the infection of the respiratory tract subsided, iodized oil instilled into the distal loop showed a small irregular lumen with two areas of constriction in the transverse colon. The distal portion of the colon or rectum ended in a conical constriction that was connected to the neck of the bladder by a fine filiform tract. After the demonstration of the rectovesical fistula, the distal loop was closed and replaced. The subsequent course has been uneventful, and further investigation and plastic operations will be undertaken later.

CASE 13.—B. S., a white boy, was sent to Charity Hospital of New Orleans two days after birth, in April 1943, with a diagnosis of imperforate anus. He was greatly distended and dehydrated, vomited excessively and appeared moribund. Examination showed probable pneumonitis. There was an icteric tinge to the skin; the saliva was yellowish, and there were hemorrhages in the conjunctivas. Only a small dimple and a small tag of skin marked the anal site. There were five fingers on each hand but no thumbs. Roentgen examination of the inverted infant showed the gas bubble 1.5 cm. from the expected anal site. After preliminary infusion of isotonic solution of sodium chloride and blood, the rectal pouch was located by perineal dissection, mobilized, brought down, sutured to the edges of the skin and opened. A rectourethral fistula was encountered and closed. The urethra was inadvertently divided and was repaired. The postoperative condition was poor, and the baby died six hours later. An autopsy was not secured.

CASE 14.—R. T., a white boy 2 days old, was admitted to the Charity Hospital of New Orleans after home

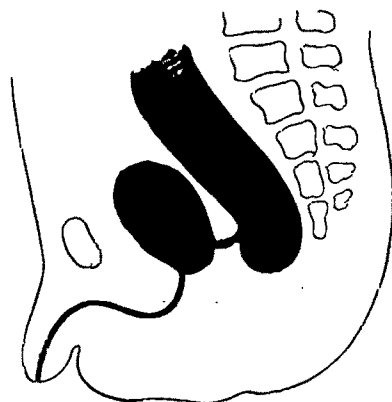


Fig. 5.—Diagram of the condition in case 14; rectal anomaly of type 3, with rectovesical fistula.

delivery, in October 1943, when it was discovered that he had no anal opening. He had vomited three times. On admission he did not appear ill or dehydrated and had no fever. His abdomen was distended but soft, and peristalsis was hyperactive. In the perineum there was a small ridge with a dimple at the anal site; no other abnormalities were noted. Roentgen examination of the inverted infant showed the rectal pouch to be 9 cm. from the anal dimple. The urine was brown and contained meconium and lanugo hairs. A Devine colos-

tomy was made in the transverse colon. Subsequently, cystourethrograms made after injection of methylthionine chloride (methylene blue) into the distal portion of the colon established the presence of a rectovesical fistula. The colostomy has functioned well since the patient was discharged from the hospital, and plastic repair is contemplated for a later date.

CASE 15.—E. T., a white boy, was born at Charity Hospital of New Orleans in February 1943. No anus or anal dimple was present. Over the lower part of the sacrum was an indentation, and deep beneath it a bony defect was palpable. Roentgen examination of the inverted infant at the age of 12 hours showed the rectal pouch to be 4 cm. from the expected anal site. A Devine colostomy was made in the transverse colon with a good functional result, and the patient was discharged from the hospital three weeks later. At the age of 2 months he was readmitted because of vomiting and diarrhea. He was poorly developed, poorly nourished and dehydrated. The urine contained fecal matter, and cystograms demonstrated a rectovesical fistula. Six weeks after the infant was readmitted, when the area of the colostomy was revised because of increasing distention, an intra-abdominal communication between the proximal and distal loops of the transverse colon was found. The communication was closed. An infection of the urinary tract developed; and despite all supportive therapy the condition of the infant became progressively worse, and he died at the age of 5 months.

Anomalies of Types 1, 2 and 4 Combined

CASE 16.—B. R., a white boy, was born at Touro Infirmary in June 1943; an imperforate anus and a hydrocele were noted at birth. After a blunt instrument was pushed through the membrane at the anal dimple, it was assumed that continuity of the rectal lumen had been established. However, roentgen examination made when no meconium was passed indicated the gas-filled bowel terminating in a blind pouch about 3 cm. proximal to the anal marker and 1.5 cm. anterior to the sacrum. Instillation of iodized oil through the perforated anal site showed the lower pouch to be 3.5 to 4 cm. in depth, extending to the gas-filled loop, and adjacent to the sacrum. Oil passed from the rectum into the neural canal through a filiform fistula

at the level of the fourth sacral disk, and there was a fistulous communication between the sigmoid flexure and the prostatic portion of the urethra. Meconium was mixed with the urine. The infant's general condition was poor and became progressively worse. A

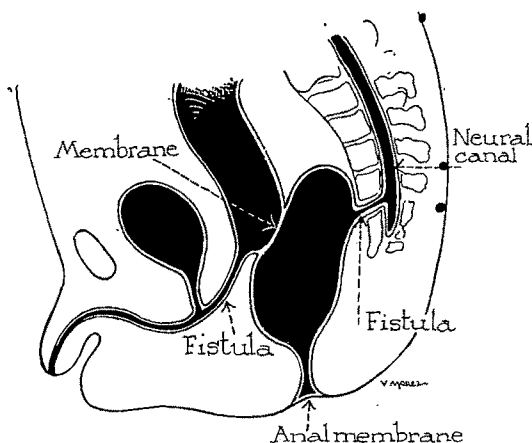


Fig. 6.—Diagram of the condition in case 16; rectal anomalies of types 1, 2 and 4, with a rectourethral fistula and a fistula between the rectum and the neural canal.

cecostomy was done to relieve the intestinal obstruction, but the patient died one day later. Autopsy verified the clinical findings, and a spina bifida occulta was also demonstrated.

CONCLUSION

This review emphasizes the high frequency of fistulas between the rectal and genitourinary tracts associated with deformities of the lower part of the rectum.

Data for some of the cases included in this study were provided by Dr. Alton Ochsner, Dr. Howard Mahorner, Dr. William P. Bradburn, Dr. Charles Bloom and Dr. Lloyd J. Kuhn.

PSYCHOGENIC INCONTINENCE OF FECES (ENCOPRESIS) IN CHILDREN

REPORT OF RECOVERY OF FOUR PATIENTS FOLLOWING PSYCHOTHERAPY

EDWARD LEHMAN, M.D.

NEW YORK

Almost every physician sees children with psychogenic problems. Too often he dismisses them with a few words about the development of good habits and a prescription for phenobarbital, a bromide or some other drug. With careful psychologic study of each child and with psychotherapy the problems may frequently be solved, the tension within the family greatly diminished and the happiness of the child and his family enhanced. Also much can be accomplished in safeguarding the child's future mental health.

Among a considerable number of children with psychogenic problems of various types seen by me in the pediatric clinic of Mount Sinai Hospital during one year, there were 4 with encopresis. This condition has been defined by Kanner¹ as "involuntary defecation which is not directly due to organic illness." Four cases of this disorder are reported here, and the subject is discussed with the aid of the available literature.

REPORT OF CASES

CASE 1.—Rose Marie, aged 7 years, was brought to the clinic by her mother because several times recently she had soiled her underwear with feces. The mother had begun training the child in control of the bowels during her first year and had had no difficulty until about a year previously, when a period of soiling had occurred. The mother complained that the girl was "nervous," meaning always restless, that she had outbursts of temper and that she frequently put her fingers into her mouth, without, however, sucking the fingers or thumb or biting the nails.

The girl's weight was slightly above average, and she was physically normal except for defective vision, which was subsequently corrected with glasses. Her intelligence was normal. While sitting on the examining table she was restless, swinging her legs back and forth.

Rose Marie had an older sister of 9 years and a younger sister of 17 months, and the 3 girls quarreled among themselves over toys and other possessions. Rose Marie shared a bed with the older sister, whom she teased and fought with about the bed clothes.

The mother was oversolicitous about the child's health habits, particularly her habits of intestinal elimination, and often administered magnesia magma. She was constantly trying to prevent the child from putting her

fingers into her mouth lest the teeth become crooked, and she did not want Rose Marie to buy sweets as she feared that the latter too might injure the teeth. She tried to force the child to drink milk, to eat cooked vegetables, although the child preferred them raw, and to take regular meals instead of eating irregularly according to her appetite. The mother was constantly frustrating the child by forbidding many things, for example, taking a toy out of doors. The child was persistent and sometimes had an outburst of temper. The mother in turn frequently lost her temper and sometimes struck the child, though usually she just "yelled" at her. The mother volunteered the information that she had been "nervous" since the last baby was born and that the pregnancy was undesired. Occasionally the mother called Rose Marie "crazy." The mother claimed that the girl wanted to receive most of her attention and that she succeeded in obtaining as much as the younger sister. However, the author's impression was that the mother did not radiate the real warmth of affection that is so important for a child's mental health.

The father, who was seen at a later visit, occasionally had a tic affecting the right eye. According to him also Rose Marie was restless and had tantrums when she was denied her way. He objected to her putting her fingers into her mouth, and while in the clinic he showed anxiety when she climbed onto the examining table. He confirmed the fact that the mother was nervous and sometimes struck the child.

Rose Marie's soiling occurred first when her baby sister was about 4 months of age. She once stated that she knew her little sister was coming before the birth, but she would not amplify this statement. As usual, after the arrival of the younger sibling the major part of the parents' attention was probably concentrated on the new baby, and Rose Marie objected to this, at times resenting the presence of the infant. This attitude was overtly expressed, between the second and third visit to the clinic, when Rose Marie was left alone with the baby while the mother went shopping. On returning the mother found her striking the baby. Rose Marie explained that the baby was noisy and that she hit it "to make it quiet."

Rose Marie competed with the baby for her parents' love, but she was at a disadvantage because the baby was younger. She therefore wished that she were again a baby. This was indicated when she expressed a wish to sleep in the crib in her parents' room, which she had used until she was 3 years old and which was now occupied by the younger sister. She added that she would not care to sleep in the crib except in her parents' room. At another visit she expressed a desire to have her father hold her on his lap and carry her about like a baby. As a result of these wishes Rose Marie, in fantasy, was a baby again and soiled her underwear as a baby soils its diapers. However,

From the Pediatric Service of Dr. Murray H. Bass, Mount Sinai Hospital.

1. Kanner, L.: *Child Psychiatry*, Springfield, Ill., Charles C Thomas, Publisher, 1935, pp. 224-227.

she was unconscious of this association until it was indicated to her.

Rose Marie was obviously attached to her father, for she frankly declared that she loved him more than her mother, and felt that he loved her. She had recently bought herself a cheap ring, which she was wearing. She acknowledged that she would like to have her mother's wedding ring and be married to her father. She evidently knew that this was taboo, as a few minutes later she said she preferred a "boy friend" named Harry. At a subsequent visit she had a fantasy that her father was married to a nurse and that she herself was married to a doctor. This indicated her liking for me and her dislike for her mother; at the same time, if the two similar elements in this equation (nurse and doctor) are canceled out, her wish to be married to the father is indirectly disclosed. This desire, freely expressed at the earlier visit, was now repressed and disguised.

At the first visit Rose Marie emphatically stated that her mother did not love her and that her mother beat her. In answer to questioning, however, she estimated that it was a couple of months since she last was struck; usually the mother just "yelled" at her. Rose Marie did not think she deserved the punishment she received. Her attitude toward her mother was further revealed at a later visit when she related that she had quarreled with a girl of her own age. They were playing "house," and the other girl wanted to be the "mother." This angered Rose Marie because she wished to play that there was no mother. In answer to questioning, Rose Marie disclosed that she would want to play that she was 19 years old and that the other girl was 17. She wanted her father to be part of this household, but she did not want her mother and sisters. The most emphatic "no" was about her mother, and the next most emphatic "no" was about the baby sister. At a later visit Rose Marie claimed that she loved both her parents equally, but she doubted whether her mother loved her even before the birth of the little sister. Of course this feeling about the mother may have been partly a projection of the child's jealousy of her.

Rose Marie related quarrels that she had had with her older sister and acknowledged that she hated her enough at times to feel like killing her. She had the same feeling about her teacher and the principal of her school. However, she received good marks except for conduct. At one visit she expressed the thought that the teacher liked her and that she was the teacher's "pet," but that the teacher was too fat (like the mother when pregnant) and "yelled" at the children and even pulled their hair. Therefore at a later visit she declared that the teacher "stinks."

Rose Marie exhibited fear of death when she recalled the loss of her uncle and when she told that she once saw a dead man and ran away. She was also afraid of "dead rats" and "dead cats," perhaps because she had a repressed unconscious urge to kill her baby sister.

The child had a frequently repeated dream in which a man kidnapped her. The man was roughly dressed, like a tramp she once saw in the neighborhood. One may suspect that the man who stole her was her father disguised.

After her first visit to the clinic there was no recurrence of the soiling, and at the end of six months, during which she was seen nine times, Rose Marie was free of her other nervous symptoms. By the end of ten months the jealousy with unconscious wishes for death and the overt aggression previously directed toward the baby sister had been replaced at times by mothering. When the mother struck the baby while training her, Rose Marie would immediately kiss and feed her. When

she played "house," she at times pretended that the younger sister was her own child and included the baby as well as her father in her fantasied home. The mechanism of such a change, in which an attitude (hate) is replaced by its antithesis (love), is termed reaction formation. Levy² included mothering among the manifestations of sibling jealousy. At the end of two years Rose Marie was well adjusted and free from all nervous symptoms. However, during this time her attitude toward her family, made manifest by the way she played "house," had undergone the series of changes briefly indicated in the accompanying table.

Rose Marie's Attitude Toward Her Family as Revealed in Playing "House."

Date	Members of Fantasied Home					
	Rose Marie	Father	Mother	Older Sister	Baby Sister	Others
5/22/42	+	+	—	—	—	Girl friend
2/10/43	+	+	—	—	+	
4/14/43	+	—	+	—	?	
6/15/43	+	—	—	—	—	Boy friend
10/27/43	+	—	—	—	+	Her own baby

+ Signifies that the member was included in the fantasied home.

— signifies that the member was rejected from the fantasied home.

Psychotherapy in this case consisted in making Rose Marie fully conscious of her fantasy of being a baby, her resentment of her two sisters, her jealousy of her mother and her love of her father. At the same time the parents, particularly the mother, were made conscious that they were often unnecessarily frustrating the child's wishes and that in their efforts to follow rules of health they were oversolicitous about the child's physical health to the detriment of her mental health. Also, as a result of treatment the mother on her own initiative tried to make Rose Marie feel as much loved as the baby.

CASE 2.—Bertha, who was 7½ years old when she was brought to the clinic, had slept in her parents' bedroom until she was 5½. She was the youngest of 4 children and the only patient in this series with incontinence plus obstipation (obstipatio paradoxa). The mother displayed an obsession about the functioning of the child's bowels shortly after her birth. Suppositories, liquid petrolatum, magnesia magma and other cathartics had been employed constantly. The mother had succeeded in training the child when she was between 2 and 3 years old by placing her on the pot every half-hour, even when on the street. However, shortly after starting school Bertha had increasing constipation plus frequent small involuntary movements. She was admitted to Mount Sinai Hospital, where it was noted that her abdomen was moderately distended with palpable loops of bowel, that her rectum was filled with hard, firm fecal impactions and that there was severe irritative dermatitis around the anus. The impaction was relieved during the first week that the child was in the hospital by frequent administration of oil enemas and digital loosening of the stool in the rectum. During the remainder of her stay in the hospital, while she was separated from her mother, the child's bowels functioned normally and regularly. Roentgenograms of the colon and the entire gastrointestinal tract were normal, as were various laboratory data, including the

2. Levy, D. M.: Studies in Sibling Rivalry, Research Monograph no. 2, New York, American Orthopsychiatric Association, 1937.

Wassermann reaction. Her basal metabolic rate was reported to be subnormal, but there was no increase in the blood cholesterol or blood lipids. Daily, administration of 1 grain (0.06 Gm.) of thyrcid was started, but since there were no apparent clinical results it was discontinued after several months, when the girl was referred to me because of a recurrence of soiling.

Bertha was unwanted before birth, and even now her mother expressed little warmth of affection, saying "Since she is here, let her live." On another visit the mother volunteered that sometimes when she was annoyed she felt like killing the girl. The child in turn obstinately refused in the clinic to express any love for the mother. The latter was domineering, while the father had a mild disposition. Bertha was more attached to him, though of all her family she now loved her elder brother best. The mother demanded implicit obedience and unnatural quiet from the child, nagged her to go to the toilet and refused to give her various foods eaten by the rest of the family. At any resistance or disobedience on Bertha's part the mother was apt to lose her temper and to scold and strike the child. At times Bertha rebelled against the punishment, and then the child and mother would strike and "curse" each other. The mother had an obsession for cleanliness; she did not even permit Bertha to play on the street lest she become dirty. To such a parent soiling was particularly annoying. Soon after her marriage and long before Bertha was born, the mother had lost both parents and a brother and sister in a fire in a tenement house. Bertha had often heard of this tragedy, and it is therefore not surprising that the girl had a fear of fire, perhaps partly caused by an unconscious wish that her mother should similarly meet death.

The mother had only one friend, a neighbor, and by keeping Bertha in the house she gave the child practically no opportunity to have companions of her own. The mother permitted none of the children to bring friends into the home, because she feared something might be broken. The siblings were considerably older than Bertha; there were 2 brothers, who were 14 and 17 years of age and a sister 19 years old who was said to have a mental age of 8 years. The mother had a fear that this older girl would be seduced if she ever spoke to a boy, and to prevent this she placed her in an institution for mentally defective persons for about a year. She was now home again for a few months. The mother often tried to compel obedience and cleanliness from Bertha by frightening her with threats of placing her too in an institution. Encopresis was precipitated by starting school, and this event must have been equivalent in the child's mind both to placement in an institution and to desertion by the mother. The child's anxiety over such a desertion was also demonstrated in the clinic by extreme panic when it was suggested that the mother leave the room so that the child could be interviewed alone. For months after this incident the child would utter hardly a word in my presence, though she was talkative elsewhere. The persistent refusal to talk was due to transference³ and was a repetition, with displacement to another field, of her refusal to have stools at her mother's command. Her action exemplified the situation described by

Bergler⁴ in which "thoughts are made the equivalent of feces and withheld." During the period of silence she showed a friendly attitude and a desire to impress me by having her father bring her excellent report from school to the clinic.

Her obstipation expressed her rebellion, while the continence expressed the conflict between her urge to comply with the mother's demands and her aggressive resentment of the mother's acts and attitudes. Bertha's resistance to her mother's command that she have stools persisted even after the passage of feces. The child still attempted to retain the stool by holding it between the buttocks, thereby producing perianal dermatitis. Another factor was Bertha's extremely intense desire for a baby, which she manifested in play fantasies and by mothering three neighbors' infants. According to Freud⁵ infants and feces are equated in the unconscious mind and the small child commonly infers that birth occurs by ways of the anus. Therefore, one may assume that, although Bertha's obstipation was originally a reaction of revolt, it was later partly sustained by the unconscious thought "I will make a baby by holding my stools till I have a big belly like Mrs. A's, Mrs. B' and Mrs. C's just before they had babies." When given this interpretation, the child replied that whenever she received enemas for an attack of obstipation her sister remarked that Bertha was having a baby. Bertha also stated that an infant is born covered with "food." I was never possible to assay how great a role ana erotism played in this child. It was apparent, however, that Bertha's symptoms were due chiefly to unconscious revolt.

Although Bertha was clean and free from obstipation after her first visit, with voluntary movements of her bowels about twice a week, there were a number of recurrences of dirtying. Such an attack occurred when Bertha was excluded from school for pediculosis capitis and the mother, to aid the cure of this condition, had Bertha's long hair cut twice to a boyish length. By coincidence the girl was summoned to the follow-up clinic at the same time, and she feared that she would be hospitalized again, particularly since the mother was once more threatening placement of the child in an institution. On one occasion Bertha apparently had encopresis without obstipation, just as the other children in this series did. The attack lasted exactly the two weeks that the mother was in the hospital for an operation. The mother's absence from home probably aroused in the child both anxiety over the seeming loss of this parent and feelings of guilt, which were caused by the apparent fulfillment of death wishes that she directed at her mother.

Therapy was handicapped by the frequent failure of the mother to keep appointments when the soiling ceased and by the obstinate silence of the child. For months treatment was usually limited to observing the child's actions, conversing with the parents in the child's presence and giving the parents and the child interpretations. It was necessary to prove to both mother and child that along with the hate that each bore the other there existed a considerable admixture of unconscious love. It was extremely difficult to modify the mother's

4. Bergler, E.: On the Resistance Situation: The Patient Is Silent, *Psychoanal. Rev.* 25:170-186 (April) 1938.

3. Freud, S.: Further Recommendations on the Technique of Psycho-Analysis: Recollection, Repetition and Working Through, in *Collected Papers*, ed. 3, published by L. Woolf and V. Woolf, London, Hogarth Press, 1942, vol. 2, pp. 366-376.

5. Freud, S.: On the Sexual Theories of Children, in *Collected Papers*, ed. 3, published by L. Woolf and V. Woolf, London, Hogarth Press, 1942, vol. 2, pp. 69-71; On the Transformation of Instincts with Special Reference to Anal Erotism, *ibid.*, pp. 164-171.

rejecting attitude, and it is yet uncertain whether a permanent cure of this child was attained. However, psychotherapy produced worth while improvement.

CASE 3.—Bobby, an only child 6½ years of age, was brought to the clinic by his grandmother because he both wet and soiled his clothes and was restless and "nervous." Nocturnal enuresis occurred only occasionally. The enuresis may have been of longer duration, but the encopresis had begun two years previously, about the time the child's parents separated. According to the grandmother the father drank and struck the mother. Bobby remembered nothing of this, not even that he had ever lived in a home with both his parents or that he had slept in a crib in their room until the separation occurred. Now he was spending five days a week with his grandmother. Every week-end Bobby spent with his mother, sharing her bed; the rest of the week she was working. Bobby had seen his father once a week until the latter went into military service. At Christmas time, while helping to pack cookies for the absent father, Bobby felt sad and cried. In fact, Bobby cried frequently, and at times he said he wished he would die. However, he was unhappy chiefly because he could not live with his mother seven days a week. Although Bobby at first claimed that both his parents loved him, he later said he was not sure of even his mother's love because she did not have him with her all the time. Once he said he was a "traitor," and when he was questioned he referred the self condemnation to his playmates. However, I related the feeling of guilt to his attitude toward his father; Bobby had his mother to himself, even though only for two days a week, not sharing her now with the father. Bobby had a fear of the dark. He dreaded injury, and also, since he had witnessed the sudden, unexpected loss of an uncle about six months previously, he dreaded death. The fear of death may have been based on a death wish directed at his rival, the father. Such aggressive fantasies were disclosed when he stated that he had received a postal card from his father but that the handwriting was unnatural and that therefore the father had injured his finger or perhaps had cut off his finger.

The grandmother, with whom Bobby spent most of his time, worried that she might "spoil" him. She tried to force him to eat, even fed him, and sent him to bed for not eating. She tried to prevent him from being a baby and nagged him frequently to go to the toilet. She continually tried to stop him from putting his fingers into his mouth and urged him to talk less rapidly. She attempted to establish a routine for him, punctual to the minute, and when she was unsuccessful in these efforts she spanked him.

Nothing could be done about Bobby's broken home; and since only the grandmother could be interviewed it was possible to influence only her attitude toward the child. However, Bobby was made to realize some of his unconscious feelings, and he volunteered that I was the only physician he had seen whom he could understand. After his fourth visit Bobby ceased wetting and soiling himself although he was discontented and unhappy because of his broken home. Frequently, while playing, Bobby tied toys and other objects together, an act that was interpreted as symbolizing his desire for more binding family ties.

CASE 4.—Ada, 6 years of age and next to the youngest of 6 children, had been soiling her underwear almost continuously since birth, but only by day. There was never any enuresis. The child received little maternal care during her first year because of illnesses of her mother and other members of the family. As a result she was cared for by neighbors and various

relatives and never learned to speak Italian, her mother's language. With training, cleanliness was achieved when she was 3 years old, but after the birth of a sister, Betty, one month later, Ada relapsed and soiled herself continuously until she came under my care. Ada felt that Betty received the major share of attention and love from the parents, other members of the family and visitors. The 2 children quarreled over their possessions, of which also Ada felt she never received a fair share. Ada frequently struck Betty as well as her other playmates. Many times Ada had complained, "Nobody in this family likes me," She would often cry without any reason apparent to the family. There were one or two neighbors who had been motherly to her, and her sister Philomena, aged 13 years, had acted in a maternal manner. However, like many misguided mothers, Philomena tried to compel obedience from Ada by frightening her with ghosts, shadows and the dark. Ada had enjoyed kindergarten but not her present school work, although she liked the teacher. School was the only place where she never soiled herself.

During the first few visits the foregoing facts were ascertained, and Ada was made conscious of her reactions to them. Then for the first time I saw and spoke to the mother. The latter was obviously aggressive and antagonistic. She demanded strict military discipline from the child, and she had punished her with blows and by putting her in a cellar and had frightened her with the threat of a "deeper cellar." She felt that the neighbors spoiled her children. On being questioned the mother denied that she loved Betty more than Ada, but in the mother's presence Ada insisted that this was so. After the mother became conscious that she was acting like a dictator in her home and after she acquired a better understanding of Ada, her attitude toward the child changed radically for the better. The latter at once stopped soiling (after six visits to the clinic), showed a friendly attitude toward Betty, ceased to fear shadows and ghosts and, as a token of reconciliation, began to speak Italian to the parents. As a result both Ada and her mother were much happier.

Although the improvement in the relations between Ada and her family was permanent, after three months she again began to dirty her underwear with feces. The onset of the relapse was abrupt, and by questioning Ada it was discovered that the recurrence of soiling followed immediately after she had chanced to witness her parents in coitus. She denied any previous similar experience, but this was probably an untrue statement, the result of repression. Although it may be assumed that Ada originally had the "sadistic conception of intercourse" typical of early childhood,⁶ she now correctly interpreted what she heard and saw not as an act of violence but as an act of love. However, she was jealous because, to her, the act indicated that both her parents loved each other more than they loved her. Ada would have liked to replace her mother in this act with the father; but she would have preferred even more to take her father's role with the mother, and she assumed the father's position, on her knees, whenever speaking of the incident. She also revealed that she had attempted to duplicate the parents' act with Betty. She denied that she had passed feces while observing the intercourse of her parents, though it is possible that she may unconsciously have felt that her father was defecating during the act. Ada was made fully conscious of the interpretation of her reaction, but there was only slight improvement of the soiling.

Finally, however, it was discovered that the dirtying was due to anxiety generated by a phobia. The family reported that Ada passed feces only when she heard an air raid siren or a fire engine. The two stimuli which excited anxiety were associated because fire engines are equipped with sirens, which, however, are unused since the installation of air raid sirens to avoid confusion. At a fire, according to Ada, everything either consumed by the flames or damaged by the firemen's efforts is destroyed by the fire engine. On her third visit Ada recalled an old dream dating back one or two years. In this dream she was on a porch and watched a fire engine drive along the street. One may suspect that the porch was the crib with sides like a porch railing that she had occupied in her parents' bedroom until she was 3 years of age and that the fire engine driving along the street symbolized in her dream her parents' coitus, which she already had witnessed from her crib before she reached the age of 3. Apparently this dream had supplied the chief object of anxiety employed later in her phobia. Therefore, because of the obvious symbolism and because the relapse started immediately after Ada observed her parents in intercourse, the interpretation was given that the siren equaled the mother in coitus because of similarity in the sounds emitted, while the fire engine was the father in coitus. Immediately after this interpretation was made all soiling ceased, ending a relapse that had lasted over three months, during which period the mother could be persuaded to bring Ada to the clinic only six times. Since then (ten months) Ada has always been clean and is no longer "scared" by the air raid siren or by the fire engines. At a later visit the child drew a fire engine with two people on it; so a final interpretation was given that the fire engine was the two parents joined in coitus, and Ada accepted this meaning with a smile.

TERMINOLOGY

The term encopresis was first coined in 1926 by Weissenberg,⁶ who regarded the disorder as analogous to enuresis. Schilling⁷ in 1891 used the term defecatio involuntaria juvenilis. Before Weissenberg introduced the term encopresis, the condition was included under incontinentia alvi. Now, however, the last-mentioned term is usually reserved for fecal incontinence caused by injury to or disease of the anal sphincter, the rectum or the nervous system, including the nerves of the anal region, or by stupor or coma, including epileptic convulsions, or general debility. Obstipatio paradoxa, a term employed by Jekelius,⁸ designates encopresis with severe obstipation, which results in enlargement of the abdomen with palpable fecal masses, overdistention of the rectum with hard feces and usually perianal dermatitis. The term paradoxa refers to the simultaneous existence of both obstipation and incontinence.

6. Weissenberg, S.: "Enkopresis," *Ztschr. f. Kinderh.* **40**:674-677, 1926.

7. Schilling: Unwillkürliche Stuhlentleerung der Jugend, *Deutsche Med.-Ztg.* **12**:691, 1891.

8. Jekelius, E.: Incontinentia alvi im Kindesalter, *Arch. f. Kinderh.* **109**:129-138, 1936.

CAUSATION

Some authors⁹ have published reports of encopresis in children without giving thought to psychic factors. Ostheimer¹⁰ in 1905 showed his lack of insight when he wrote, "The cases in which some antecedent illness is known to have been the cause are easily understood; but in those children in whom incontinence of feces alone or incontinence both of feces and of urine occurred, the anal sphincter must have been affected, even though digital examination failed to elicit any relaxation of this muscle." In some cases reported by other authors¹¹ psychic factor were so glaring that they were mentioned briefly and even remedied, but the improvement or cure obtained was attributed to some drug, diet or regimen that had also been prescribed. Marfan¹² reported on 10 schoolboys with encopresis of whom 6 had a positive Wassermann reaction. He therefore suggested that one should search for signs of congenital syphilis in such patients and that even if none were found one should attempt antisyphilitic therapy. However, as Glanzmann¹³ pointed out, there can be no direct relation between syphilis and encopresis. The coincidence may perhaps be explained by the greater frequency of syphilis in parents of neglected children living in bad environments. As Jekelius⁸ stated, every attack is functionally determined and curable in principle. Burns¹⁴ also stated that encopresis is primarily a psychogenic disorder. Similar views have been expressed by Shirley,¹⁵ Glanzmann,¹³ Kanner,¹

9. (a) Rivière, A.: Incontinence fécale par regorgement chez une fillette de douze ans, *Med. mod.* **9**:308-309, 1898. (b) Hungerland, H.: Chronische Obstipation als Ursache für Incontinentia alvi, *Arch. f. Kinderh.* **108**:43, 1935. (c) Fucci, C.: Un caso di defecazione involontaria, detta degli scolari, *Prat. pediat.* **13**:179-183 (March) 1935. (d) Wallace, A.: Incontinence of Feces, *St. Barth. Hosp. Rep.* **24**:260, 1888. (e) Priesel, R., and Siegl, J.: Chronische Obstipation als Ursache für Incontinentia alvi, *Arch. f. Kinderh.* **107**:133-136, 1936.

10. Ostheimer, M.: Incontinence of Feces in Children, *Univ. Pennsylvania M. Bull.* **17**:405-407 (Feb.) 1905.

11. (a) Griffith, J. P. C.: Nervous Incontinence of Feces, *Arch. Pediat.* **16**:416, 1899. (b) Hartsilver, J.: Incontinence of Faeces in a Young Girl, *Lancet* **2**:427-428 (Aug. 24) 1935. (c) Oegg, H.: Ein Beitrag zur Beurteilung und Behandlung des Krankheitsbildes der Incontinentia alvi im Kindesalter, *Monatschr. f. Kinderh.* **79**:230-235, 1939.

12. Marfan, A. B.: La défécation involontaire des écoliers, *Presse méd.* **42**:1-2 (Jan. 3) 1934.

13. Glanzmann, E.: Zur Psychopathologie der Encopresis, *Ztschr. f. Kinderpsychiat.* **1**:69-76 (Aug.) 1934.

14. Burns, C.: Encopresis in Children, *Brit. M. J.* **2**:767-769 (Nov. 29) 1941.

15. Shirley, H. F.: Encopresis in Children, *J. Pediat.* **12**:367-380 (March) 1938.

schachter,¹⁶ Thom,¹⁷ Pearson¹⁸ and Morichau-beauchant.¹⁹ Certainly any one who carefully studies children with encopresis, works out the psychogenesis of each case and observes the response to psychotherapy must conclude that this disorder is of psychic origin.

Pearson^{18a} stated: "In many cases of soiling there is definite evidence of lack of parental love for the child." Encopresis may occur if the child feels unloved, even by only one of its parents, particularly the mother. Unfortunately some parents are not capable of loving a child wholeheartedly. They unconsciously betray this fact, which is easily sensed by the child. Lack of parental love was present to various degrees in all 4 of the cases reported here, and it is a basic factor in a variety of situations in which encopresis occurs. Incontinence was precipitated in 2 of the 4 cases by the birth of a younger sibling who became the recipient of the largest share of the parents' attention. Similar sibling jealousy occurred in a case reported by Shirley,¹⁵ and the same situation was mentioned by Fenichel²⁰ and by Pearson.^{18a} One of my 4 patients attempted to regain the parents' attention through the mechanism of an unconscious fantasy that she was again an infant and therefore spoiled herself.

Parental love is surely lacking when a child has never had a real home with loving parents and when a child has a good home and then loses it. Schachter¹⁶ stated that encopresis occurs frequently in asylums for illegitimate children and orphans. Pearson^{18a} stated. "It is a common experience for foster mothers to find that a well-trained young child loses all his training when placed in the new home, only to become clean again when he starts to be fond of the new mother." According to Anna Freud,²¹ when by

separation a child loses its relation to the mother or nurse who is responsible for the establishment of cleanliness, it also loses the pleasure in fulfilling the requirement. The breaking up of a family precipitated encopresis in 1 of the patients described here, and in only 23 per cent of the cases reported by Jekelius⁸ was the family intact. Burns¹⁴ stated that in Britain during the present war encopresis is fairly prominent among the problems that result from the transfer of children from cities in danger of bombing to the safety of rural foster homes.

Shirley¹⁵ stated that it is an outstanding fact that many children with encopresis are from unhappy homes, in which parental love is frequently lacking. This may be true of stepchildren and of children with alcoholic, highly neurotic or psychotic parents. Sometimes the unhappiness is due to extreme attitudes and ideas of the parents. The mothers of at least 2 of my patients were extremely domineering and despotically demanded strict discipline. They were feminine dictators who expected their children to respond with the alacrity of soldiers. Such mothers may constantly nag a child, directing every minute detail in his life, not realizing that they are destroying the capacity of the child for independent action and initiative. The mother usually does this because of anxiety, perfectionism or a desire to relive her life vicariously in the child's life or just for her convenience; however, she usually rationalizes her actions with the excuse that she does not wish to "spoil" the child. The father in such instances is usually weaker than average. Another extreme attitude, reported by Fowler,²² Rotch,²³ and Schachter,¹⁶ may be assumed by a father who has his own pedagogic ideas. He institutes an educational regimen that is calculated to develop an infant prodigy. For example, Fowler²² reported on a 7 year old boy whose father was extremely ambitious in regard to the son. Education was started when the boy was 4 years of age, and the pressure was gradually increased. When he was 7 years old, the boy's studies began before breakfast and included Spanish, German, French and music in addition to the ordinary curriculum. Fowler stated that "under such conditions it is not to be wondered at that something gave way, and fortunately for the brain, it was the sphincter ani."

Marfan¹² designated this disorder "involuntary defecation in school children." In 2 cases reported by Shirley¹⁵ encopresis began when the

16. Schachter, M.: L'énurésie et l'encoprose diurne de sécoliers, *Semaine d. hôp. de Paris* 10:254-258 (April 30) 1934.

17. Thom, D. A.: *Everyday Problems of the Everyday Child*, New York, D. Appleton-Century Company, Inc., 1934.

18. (a) Pearson, G. H. J.: *The Psychiatry of Childhood*, in Christian, H. A., and Mackenzie, J.: *Oxford Medicine*, New York, Oxford University Press, 1936, vol. 7, pp. 172-173. (b) English, O. S., and Pearson, G. H. J.: *Common Neuroses of Children and Adults*, New York, W. W. Norton & Company, Inc., 1937, pp. 27-35 and 112-117.

19. Morichau-Beauchant, R.: *False Incontinence in Children*, *Paris méd.* 12:83-89 (July 22) 1922.

20. Fenichel, O.: *Outline of Clinical Psychoanalysis*, New York, W. W. Norton & Co., Inc., 1934, pp. 25-26.

21. Freud, A.: *Introduction to the Technic of Child Analysis*, *Nervous and Mental Disease Monograph* 48, Washington, D. C., *Nervous and Mental Disease Publishing Company*, 1928, p. 46. Freud, A., and Burlingham, D. T.: *War and Children*, New York, *Medical War Books*, 1943, pp. 73-76 and 160.

22. Fowler, G. B.: *Incontinence of Feces in Children*, *Am. J. Obst.* 15:984-988 (Oct.) 1882.

23. Rotch, T. M.: *Pediatrics*, ed. 5, Philadelphia, J. B. Lippincott Company, 1906, p. 798.

children started school and was present only when they were in school. Glanzmann¹⁸ mentioned a child who had difficulty with arithmetic and had incontinence of feces only in school. Schachter¹⁶ stated that encopresis may be a reaction against scholastic authority. Shirley¹⁵ had 1 case in which the symptom occurred in a child at boarding school and ceased when the child returned home. He also noted that 18 of 25 children of school age with this disorder had difficulties at school. There were other important causative factors in 1 of the cases reported here, but encopresis was precipitated by starting school, an event which seemed to the child to be desertion by the mother.

In cases reported by Shirley,¹⁵ and Kanner¹ and in 2 of the cases reported here, the mother was excessively preoccupied with the child's intestinal functions. From the child's early infancy the mother had constantly employed cathartics and enemas, because of her anxiety concerning possible harm from lack of frequent intestinal evacuations. Training in habits of defecation may be started too early or may be too insistent. The mother of 1 of my patients placed the infant on a pot every half hour, not only at home but even in the street.

Usually after the onset of encopresis the mother continuously nags the child, forcing him to go to the toilet many times a day. This only increases the pressure on the child and tends to perpetuate the incontinence. Also it usually proves ineffective, as the child may soil himself immediately after leaving the bathroom. In 1 case constant nagging by a domineering and rejecting mother resulted in a reaction of revolt. The child unconsciously refused to defecate as the mother ordered and tried tenaciously to retain the feces, which resulted in the syndrome termed by Jekelius⁸ *obstipatio paradoxa*. With this syndrome the abdomen may be much distended, and fecal masses may be palpable. However, the child cannot retain his feces indefinitely, and soon there is incontinence with the loss of a small piece of fecal material at a time. Even then the child still probably seeks to retain its feces, holding the pieces in the anal fold, between the buttocks, thereby producing the macerated perianal skin apparently found only with incontinence of this type. Cases of *obstipatio paradoxa* have been reported by a number of authors. Priesel and Siegl^{9a} and others claim that regular emptying of the intestinal tract of such patients with enemas and cathartics effects a cure. Treatment of encopresis of this type should perhaps be initiated by such measures, but one should never omit psychotherapy.

In the unconscious mind, according to Freud,⁵ feces are equated principally with gift, infant and

penis. Alexander²⁴ utilized the gift significance of feces to explain severe constipation. His general formulation may appropriately be applied specifically in the case of *obstipatio paradoxa* reported here. The child's subconscious "reasoning" was as follows. "Inasmuch as I do not receive love from my mama, I do not need to give her my stool." In such instances the feces is regarded by the child as a valuable possession perhaps even as a part of himself.¹⁸ Such a gift to the mother would be a token of the child's love, which in the case referred to was likewise withheld. At the same time a negative attitude toward the intestinal contents and toward the mother may be expressed by encopresis. Alexander reconstructs the attitudes as "Well, if I have to give, by all means you may have it but nothing better than excrement." In expressing the attitude of my patient with *obstipatio paradoxa* one may add, "and since my mama is so obsessed by cleanliness, let the stool go into my clean panties." The apparent contradiction in the child's attitude toward his feces, namely that they are regarded at the same time as precious and valueless, merely reflects the parent's attitude toward defecation. Children are congratulated for adequate and satisfactory defecation at the right time but are scolded and treated with disgust when they soil themselves.

In the case of encopresis with obstipation described in this report, although the tenacious retention of feces was originally a reaction of revolt against a domineering and rejecting mother, it was later partly maintained by an additional factor, the girl's intense desire for a baby to mother. By holding her stools she was unconsciously striving to attain the greatly enlarged abdomen that had been evident to her in various neighbors before they had babies. In this case obstipation was the result of the equation of infant and feces in the unconscious mind and of the theory common with children that birth occurs through the anus.

According to the literature another cause of *obstipatio paradoxa* is anal erotism. Freud²⁵ mentioned "children who like retaining their excreta till they can derive a voluptuous sensation from their evacuation." An adult analyzed

24. Alexander, F.: The Influence of Psychologic Factors upon Gastro-Intestinal Disturbances, *Psychosom. Quart.* 3:529-539 (Oct.) 1934.

25. Freud, S.: A Phobia in a Five-Year Old Boy, in *Collected Papers*, ed. 2, published by L. Woolf and V. Woolf, London, Hogarth Press, 1942, vol. 3, p. 250; *Infantile Sexuality: Three Contributions to the Theory of Sex*, in *The Basic Writings of Sigmund Freud*, translated by A. A. Brill, New York, Modern Library, 1938, pp. 589-590.

Stekel²⁶ reported that as a boy he was accustomed to hold back his stools a long time. When he played with them by propulsion and propulsion through the anal sphincter, thereby obtaining a feeling of pleasure. While doing this he often soiled himself, for which he received corporal punishment. Glanzmann¹³ reported on a girl of 9 years with an almost identical history. Morichau-Beauchant¹⁹ recorded 3 cases in which the conditions were believed to be similar. This behavior is regarded as a substitute for masturbation. However, one may infer that in such cases the stool is equated with the penis. Fenichel²⁰ says that frequent incontinence of feces is possible only if the person is highly anal erotic.

Anxiety can produce diarrhea and may be an important factor in fecal incontinence. Anxiety may certainly result from lack of parental love, among other things. In one of Shirley's¹⁵ cases involuntary defecation was caused by the boy's fear of injury by his father. Burns,¹⁴ referring to encopresis precipitated by present war conditions, said that the disorder is "a protest against an inimical and threatening environment." Jekelius⁸ classified 40 per cent of his patients as "Angstkinder." He stated that they were shy, anxious, ashamed of their incontinence and afraid of the dark and of dogs and that 15 of 40 children in this group had a fear of going to the toilet alone.

Abnormal fears favor retention or incontinence of feces. For example encopresis may be caused directly by toilet phobia. One child reported on by Kanner¹ sought to avoid using the toilet because he feared being washed down the drain pipe as the feces were. The fear of the loss of feces because this seems to the child to be a loss of a part of its body may become a phobia.^{18a} Encopresis may be produced less directly by anxiety generated by phobias unrelated to defecation. In 1 case reported here a phobia resulted from witnessing the parents in coitus. Freud²⁷ reported a phobia (with encopresis) based on such an incident and Fenichel²⁰ regarded this experience as a common cause of phobias in children. To avert such psychic trauma no child should sleep in the parents' bedroom.²⁸ According to Melanie Klein,²⁹ even a

baby that seems to be asleep may perceive the parents' intercourse in a dim way, so that a vivid but distorted memory of the experience remains in its unconscious mind and has harmful effects on the infant's future development. A child is practically sharing its parents' bedroom when it sleeps in an adjoining room with an open door or a glass-paneled door between. Unfortunately such sleeping arrangements are extremely common, because of economic conditions or parental anxiety. Even if the child has its own room, opportunity for such psychic trauma may occur on trips or during an illness of the child, when it may temporarily share the parents' bedroom.

Encopresis has been described as a spite reaction. A boy described by Pototzky³⁰ always soiled himself two hours after a scolding (never right away) and "felt triumphant" over the parents' rage. As a rule, however, such a spite reaction is unconscious, and it is a mistake to regard the act as voluntary misconduct which deserves punishment. Punishment usually serves only to aggravate the disorder. Stier³¹ perhaps overemphasized the role of sadism in encopresis. However, as has been pointed out by Melanie Klein,³² a small child may in fantasy employ his excreta for aggressive and sadistic purposes including revenge. Jekelius⁸ classified 20 per cent of his patients as "Bösheits- oder Aggressionskinder." He stated that they opposed home or school, that they were against their parents, siblings and playmates, that they destroyed or threw everything and tore their own clothes and that they defecated in their underwear or bed, often right after being put on the toilet, as if for spite. He also stated that children of this aggressive type are prone to have obstipatio paradoxa. Kanner¹ says it is especially interesting to note the frequent occurrence of temper tantrums in connection with encopresis.

However, children with encopresis exhibit not only sadistic but strong masochistic trends. Unconsciously they bring on themselves all sorts of scolding and punishment; they are treated

tioners Library of Medicine and Surgery, New York, D. Appleton-Century Company, Inc., 1938, vol. 13, pp. 795-797.

29. Klein, M.; Weaning, in Rickman, J.: On the Bringing Up of Children, London, Kegan Paul, Trench, Trubner & Co., Ltd., 1936, p. 52.

30. Pototzky, C.: Psychogenese und Psychotherapie von Organsymptomen beim Kinde, in Schwarz, O.: Psychogenese und Psychotherapie körperlicher Symptome, Berlin, Julius Springer, 1925, p. 417.

31. Stier, E.: Soiling in Children and Its Relation to Wetting, *Ztschr. f. Kinderforsch.* 30:125-144 (March 28) 1925.

32. Klein, M.: The Psycho-Analysis of Children, translated by A. Strachey, published by L. Woolf and V. Woolf and Institute of Psycho-Analysis, London, 1932, pp. 205, 230 and 281.

26. Stekel, W.: Störungen des Trieb- und Affektlebens, in *Psychosexueller Infantilismus*, Berlin, Urban & Schwarzenberg, 1922, vol. 5, p. 218.

27. Freud, S.: An Infantile Neurosis, in *Collected Papers*, ed. 2, published by L. Woolf and V. Woolf, London, Hogarth Press, 1942, vol. 3, pp. 552-563.

28. Sharpe, E. F.: Planning for Stability, in Rickman, J.: On the Bringing Up of Children, London, Kegan Paul, Trench, Trubner & Co., Ltd., 1936, pp. 14-16. Spock, B., and Huschka, M.: The Psychological Aspects of Pediatric Practice, in Blumer, G.: Prac-

with contempt and disgust, and they subject themselves to social ignominy in the family, among their playmates and at school. Nothing deters them, and they continue to "take it," thereby giving definite evidence of masochistic tendencies.

Another psychic mechanism involved in encopresis is regression, which is typified by the reaction of the patient who had a definite unconscious fantasy of being an infant again. Excessive "babying" of a child, such as may occur during a severe illness, may encourage regression. Gurewitsch³³ reported an extreme instance of regression. A 36 year old man was brought to the clinic like a bad boy by his obviously domineering wife. Until he was 14 years of age he had had incontinencia alvi and urinae in spite of blows and reproaches by his mother. The symptoms had now recurred to such an extent that the wife finally put diapers on him at night. Gurewitsch interpreted this as a regression to the status of a small child.

Involuntary defecation is of course normal in early infancy. According to Susan Isaacs³⁴ control of the bowels is commonly achieved at about 18 months, though some children will be clean earlier and many perfectly normal, happy children achieve control a good deal later than this. In the period right after the infant's training in control of defecation, when control of the bowels seems achieved, encopresis is common. According to Isaacs³⁴ "occasional breakdowns will occur with every child." She stated that "sometimes no external reason can be traced. In other cases, it is clear that a particular happening has stirred up the difficulty, for example, a change in general routine, a change from the bottle to solid food, a change in the time of the midday rest, going away for a holiday, teething, the birth of another baby, the mother's illness or miscarriage, the loss of a nurse and coming of a new one, and other such significant events." Likewise Menninger³⁵ stated that "most infants go through the experience toward the end of their anal phase of development of having occasional 'accidents' of soiling." He described a "phase of defiance" during which the infant refuses to perform on the toilet but performs at

an inappropriate time, after the parent has given up. This phase of defiance may lead to a "phase of sensual pleasure in retention." Kubie³⁶ states the belief that sullen refusal, retention and willful soiling at the time of the shift from the wearing of diapers to the use of the toilet may result because the child has been deprived of the "comfort of the cleansing rituals spread over the genitals."

Kanner¹ stated, "Persistence of soiling beyond the end of the second year of life may be due to serious mental retardation, or to lack of proper training or both." Only if a child has never been clean may a lack of training be suspected; the lack of training, however, may be fundamentally a result of neglect and lack of parental love. Seven of Shirley's¹⁵ 33 patients with normal intelligence had a history of soiling since infancy. Jekelius⁸ stated that 81 per cent of his patients were never clean, a surprisingly high figure, particularly since only 16 per cent of the children were idiots and imbeciles. Three of the 4 patients described in this report had been clean for years before the onset of encopresis. The fourth, a neglected child, first achieved cleanliness in her third year, but one month later coincident with the birth of another sibling she reverted to soiling which continued for another three years, until it was cured by psychotherapy.

Encopresis is more frequent in feeble-minded than in normal children. Of 70 patients described by Shirley¹⁵ 21 were idiots or imbeciles, 5 were morons and 10 were of borderline intelligence. However, of all feeble-minded children seen by Shirley at the Psychiatric Clinic of the Harriet Lane Home for Invalid Children, only 4.8 per cent had encopresis, including only 14 per cent of the idiots and imbeciles. Kanner¹ stated: "We have seen many idiotic and imbecile children who with good training had established good fecal and urinary habits at an early age, and again others in whom the training had had but little effect. Usually, at about five years of age, even the imbecile (and sometimes the idiotic) child had ceased to soil himself." The same psychic factors may operate in mentally defective as in normal children, but lack of training resulting from parental defeatism, neglect and lack of love is probably of great importance in the causation of encopresis in feeble-minded children. This assumption is supported by the fact that a dog has enough intelligence to be taught cleanliness. Incidentally, the author knows of a dog with well established habits of cleanliness that reverted to soiling when psychically disturbed by not being

33. Gurewitsch, W.: Beitrag zum Problem der Organneurose: Hysterische Harnverhaltung und Stuhlinkontinenz, Deutsche Ztschr. f. Nervenhe. **124**:247-257, 1932.

34. Isaacs, S.: Habit, in Rickman, J.: On the Bringing Up of Children, London, Kegan Paul, Trench, Trubner & Co., Ltd., 1936, pp. 133, 135, 147, 160 and 165.

35. Menninger, W. C.: Characterologic and Symptomatic Expressions Related to the Anal Phase of Psychosexual Development, Psychoanalyt. Quart. **12**:161-193 (April) 1943.

36. Kubie, L. S.: The Fantasy of Dirt, Psychoanalyt. Quart. **6**:388-425 (Oct.) 1937.

mitted to sleep, as it was accustomed to do, the same room with its master.

TREATMENT

Physicians who ignored the psychic basis of encopresis have employed a variety of drugs, including ergot,²² belladonna,²² atropine, strychnine,²² antisyphilitic remedies,¹² vitamin B,^{11c} and calcium,^{11c} and local treatment with ointments⁸ and suppositories.²² Some have employed faradic stimulation⁷ or "remedial exercises" of the abdominal and pelvic muscles, including the sphincter ani. All such pharmacologic and physical therapy is superfluous and non-specific; it works, if at all, by suggestion, by transference or if unpleasant by coercion, without resolving psychic conflicts and without improving the child's mental health.

The therapeutic approach described here is based on psychoanalytic insight and methods, since these have in practice been most productive of lasting results.

First the physician must establish a good relationship not only with his small patient but with the parents. Usually the mother brings the child to the physician, and she should be permitted to tell her story in her own way, usually in the child's presence, with occasional encouragement to go into greater detail when she reaches some point of psychologic importance. At the end of her story a question or two will again start her on any angle that she may have omitted. This approach gains the cooperation and confidence of parents and encourages them to become conscious of psychologic factors. From this interview one may infer much about the attitudes and character of the parent. The actions of the child during this recital and the reactions of the parent to the child must not be overlooked.

Then the child is encouraged to talk. Perhaps during the parent's recital the child has already spontaneously added details to the story or attempted to modify the account. In any event, the next step is to gain the confidence of the child, to make him feel that the physician is really a friend and not a person who will lose his temper and scold or punish as the parents or teacher may do. One must have patience and devote a great deal of time to the child. The employment of toys and a "play technic" may be helpful. After the initial timidity and anxiety have been overcome, the visits are with the child alone. Although an occasional question may expedite progress, usually the child should be allowed to say whatever comes to his mind. One should listen attentively to apparently trivial details, as they may have more significance than is at first apparent. In time the child will confide what

he remembers of past experiences, including the emotional reactions, and interpersonal relationships at home, with playmates and at school. However, a child does not realize his unconscious attitudes and therefore cannot directly tell one about them. Nevertheless, with the aid of experience, conclusions concerning these attitudes may be drawn after observing what a child says and does, how he chooses to play and what dreams and fantasies he constructs.

The final step in psychotherapy is gradually to interpret the unconscious attitudes to the child so that he is fully conscious of the reasons for his actions. This step permanently removes many of the child's psychic strains and conflicts. In the treatment of small children it is frequently necessary to relieve excessive environmental pressures, particularly those placed on the child by the parents. This is accomplished by tactfully interpreting to the parents their unconscious attitudes so far as these affect the child and by promoting in them greater comprehension of the child. However, I treated 1 patient with encopresis, precipitated by the breaking up of the family, successfully without ever seeing either parent, without affecting their attitude toward the child and without changing the status within the family. In the treatment of this disorder one must usually influence the parents to employ an attitude of kindness and love instead of strict discipline and constant punishment.

Of course a child deserves praise when cleanliness is achieved, but any efforts to induce control by offering rewards or bribes or even using a "star chart" are of questionable utility. Such short cuts may at times appear to succeed, but they are apt to result in the substitution of other symptoms for soiling without effecting any permanent improvement in the child's mental health. The proper procedure is to relieve the unconscious psychic strains and conflicts; then the child will become clean. To be more condemned, but for similar reasons, is the method of Jekelius,⁸ who, despite adequate insight into the psychic origin of encopresis, sought to coerce cleanliness by administering ill tasting drops, decreasing the number as the child improved and increasing it after a relapse. He claimed success in 60 per cent of his cases from the use of this routine alone. Aside from the element of suggestion, this method is merely punishment in a subtle form. Almost always the parents have tried punishment before consulting a physician but have usually abandoned it as useless or aggravating. An unconscious act such as encopresis should not be regarded as intentional misbehavior meriting punishment.

Obituaries

JOSEPH BRENNEMANN, M.D.
1872-1944

Dr. Joseph Brennemann died at his home near Reading, Vt., on July 2, 1944. Although he had retired from full time work a year previously, he had not given up his interest in pediatrics. He continued to spend much time editing his "Practice of Pediatrics," and carried on an extensive correspondence with many medical colleagues. During the month of April 1944 he served as visiting physician at the Milwaukee Children's Hospital. In June he read a paper before the Section on Pediatrics of the American Medical Association.

Dr. Brennemann was born near Peru, Ill., on Sept. 25, 1872. His premedical education was obtained at the University of Michigan, and his medical degree was received from Northwestern University Medical School in 1900. He served a two year internship at St. Luke's Hospital, Chicago, and then engaged in general practice on Chicago's south side. After a few years he decided to specialize in pediatrics, and in 1910 he spent several months in European pediatric clinics. For many years he was attending physician in the pediatric outpatient department of Northwestern University Medical School, was actively engaged in teaching medical students and was in addition attending pediatrician at St. Luke's Hospital and at Wesley Memorial Hospital. In 1921 he gave up these appointments to become chief of staff of the Children's Memorial Hospital, where he remained for twenty years. After his retirement from the Children's Memorial Hospital he became chief of staff of the Children's Hospital, Los Angeles, and professor and head of the department of pediatrics of the University of Southern California Medical School.

Dr. Brennemann was the recipient of practically all of the honors which pediatrics could confer on him. He was a member of the Chicago Pediatric Society, the American Academy of Pediatrics and the American Pediatric Society. He was president of the American Pediatric Society in 1930. He was an honorary member of the Society for Pediatric Research and a corresponding member of the British Pediatric Society.

It is difficult to know what qualities make for greatness in the field of medicine. That Dr. Brennemann had certain qualities which set him apart from the majority of his colleagues all who knew him will agree. He had a rare independence of mind. The new in medicine had to be subjected to the severest scrutiny not once but

many times before he was willing to accept. He never followed the crowd. In fact, he so on numerous occasions to turn his colleagues from accepting too easily the current fashionable pediatric thought. Brief reference to three particular articles will, I think, reveal his keen sight into medical trends.

In the period when "the mothers' eyes" were fixed on the scales as the final arbiter of nutrition Dr. Brennemann wrote "Psychologic Aspects of Nutrition in Childhood"; when physicians were becoming enthusiastic over new and well publicized topical applications he wrote "Vis Matris Naturae in Pediatrics," and when a physician and laity began to talk glibly of conditioned reflexes, behavior problems and complexes he wrote "The Menace of Psychiatry." This last paper, certainly the most popular of all his medical articles, brought hundreds of congratulatory letters not only from this country but from all over the world.

In spite of the wide acclaim which followed these more or less philosophical articles, Brennemann always insisted that his paper, published in 1911, entitled "Contribution to Knowledge of the Etiology and Nature of Enteric Curds in Infants' Stools" was his best piece of work. It settled a controversy that had engaged pediatricians over a number of years.

His supreme achievement, however, was editorship of and his extensive contribution to "Brennemann's Practice of Pediatrics." He was a careful and painstaking editor, feeling personally responsible for the quality of all of the articles which were submitted. This monumental work has assured him an enduring place among the great leaders in pediatrics.

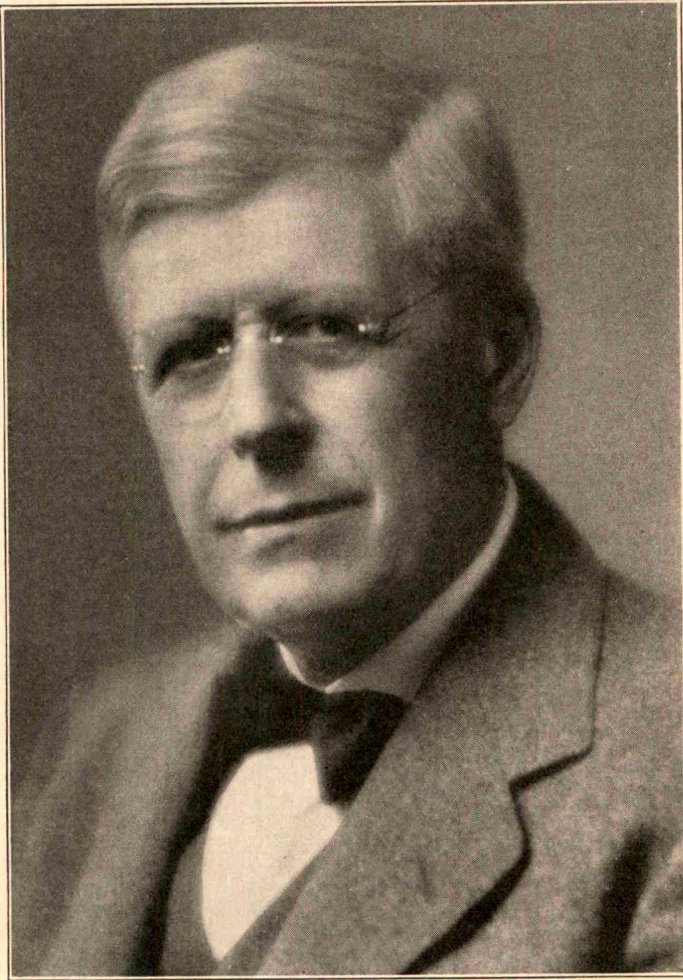
His fame as a teacher equaled or excelled that which he enjoyed as a writer. He spoke clearly in good voice, and was always accurate to most minute detail in his presentations. He had a superb gift of showmanship. He knew how to set contrasting cases off against one another and knew how to highlight the essential features which made the case worth while, and he knew the value of suspense in holding the interest of his audience.

In spite of his zeal and fierce concentration on clinical medicine, Dr. Brennemann still found time for excursions into fields far removed from his professional studies. He was an omnivorous reader. A good many years ago while spending some ten days in bed with an infection of

per respiratory tract he read in its entirety a very formidable textbook on geology. A year or so I spent an evening with him as he was passing through the city. I asked him whether he had read a certain article in a recent magazine. He said, "No, I do not believe I have come to it yet. I have the magazine with me in the Spanish edition, and I am a bit slow in reading it. I don't know why the devil a man

from his farm just a few days before his death he was complaining about the weather. He said: "It has rained all day; in fact, it has rained all week. I am beginning to feel as Noah must have felt, only he had an assurance from the Lord that is lacking in my case."

Over and above Dr. Brennemann's brilliant intellectual achievements was his solidity of character. One never doubted his sincerity. He



JOSEPH BRENNEMANN, M.D.
1872-1944

at seventy should be trying to perfect his Spanish, but anyway it's good fun." Then with a twinkle in his eye he quoted a Latin phrase—I had heard him quote it a number of times before—which being translated means, "Nothing of human interest is foreign to me." What he had said half in jest was in real truth a perfect characterization.

Dr. Brennemann's conversation, his writing and his teaching were enlivened by a gentle irony and a fine sense of humor. In a letter written

could not tolerate pretense or sham. He stood for what he believed to be right and had the courage to voice his convictions. He cared not at all for social life in the usual sense, but he was supremely happy in a small gathering of congenial friends. His friendship knew no bounds. He was no less the friend of the errand boy at the hospital or of the humblest dispensary patient than he was of his medical associates.

Yet it was the young men and women in medicine who were nearest to his heart. He

was never the "big professor." He worked *with* his residents and always insisted that he learned more from them than they from him. His attitude is exemplified in the dedication of his *Practice of Pediatrics*: "In a very affectionate sense to that keen, earnest and loyal group of young men and women whom I have tried to teach and who have taught me so much, my interns and residents of many years."

Dr. Brennemann married Bessie Darling Daniels in 1903. Mrs. Brennemann, their three daughters—Mary, Barbara and Deborah—and seven grandchildren survive him.

Dr. Brennemann's final illness was brief. He had complained of slight pain in his chest and his left arm for a few days. About twelve hours before his death the pain became so severe that his physician was called. Administration of morphine gave relief. An electrocardiogram was taken. A few hours later his physician returned with the tracings. Dr. Brennemann had just put on his glasses to look at them when he slumped suddenly and was gone. Surely it was the very last moment of his life.

STANLEY GIBSON, M.D.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

MOTOR CONTROL OF THE THORACIC DUCT. DARIO ACEVEDO, *Am. J. Physiol.* **139**:600 (Aug.) 1943.

It is inferred from these and from earlier studies at the lymph channels are contractile organs under nervous control. This contractility is one of the factors which governs the flow of lymph.

NOURSE, Cleveland.

Metabolism; Infant Feeding; Milk and Other Foods

FIELD PEAS AS A SOURCE OF PROTEIN FOR GROWTH. ELLA WOODS, W. M. BEESON and DONALD W. BOLIN, *J. Nutrition* **26**:327 (Oct.) 1943.

Raw and heat-treated Alaska field peas (*Pisum sativum*) were studied as the sole source of protein in diets for growing rats. A deficiency of methionine was found to be the principal growth-limiting factor in the proteins of the raw peas. Baking and autoclaving the field peas decreased the growth-promoting properties of the protein but did not change the amount of food ingested. Cystine added to the autoclaved peas permitted a rate of growth comparable to that with raw peas. Apparently the Alaska field pea is an excellent source of the amino acids essential for growth, with the single exception of methionine.

FREDEEN, Kansas City, Mo.

STUDIES OF THE AVERAGE AMERICAN DIET. VERNON H. CHELDELIN and ROBERT R. WILLIAMS, *J. Nutrition* **26**:417 (Oct.) 1943.

The average diet consumed by the middle two thirds or three fourths of the population of the United States prior to the use of enriched bread and flour contained approximately 1.4 mg. of riboflavin, 11 mg. of nicotinic acid and 4.9 mg. of pantothenic acid per 2,500 calories. These values are appreciably lower than the most generally accepted daily requirements. The enrichment of bread and flour increased the level of riboflavin to 1.6 mg. and of nicotinic acid to 17 mg., meeting the prevailing standards.

The principal contributors of these vitamins to ordinary diets are as follows, in the order of their importance: for riboflavin, milk, white bread, eggs and potatoes; for pantothenic acid, white bread, milk, eggs and potatoes. Tables are presented to permit the calculation of the amounts of each vitamin provided by various diets.

FREDEEN, Kansas City, Mo.

CHILD NUTRITION IN CHILE. GUILLERMO MORALES BELTRAMI, *Bol. Inst. internac. am. de protec. a la infancia* **17**:27 (July) 1943.

The nutrition of children in Chile presents, in general, the following deficiencies: (a) lack of sufficient protein; (b) lack of the fats which are most suitable for the diet of children; (c) excess of carbohydrates; (d) deficiency in vitamins; (e) deficiency in iron, calcium and magnesium, and (f) deficiency in fruits and green vegetables.

The essential reasons for the inadequacy of the average diet are the scarcity of milk, which is expensive

and not of good quality, the limited purchasing power of the average family and the lack of knowledge of nutrition and of the care of children in general.

The technical protectional services can start a campaign in behalf of rational nutrition for children by establishing a program of education in the care of children, especially in relation to nutrition, by making recommendations to the authorities who control the production of food, by recommending to the government the adoption of all measures which directly or indirectly contribute to raising the average standard of living of the population and by equipping the institutions for the assistance of children as centers for supplying the people of the working class with good milk at low cost.

EDITOR'S SUMMARY.

PRESENT NUTRITION PROBLEMS OF THE UNITED STATES AS THEY AFFECT CHILDREN. Prepared by the Children's Bureau, United States Department of Labor, *Bol. Inst. internac. am. de protec. a la infancia* **17**:47 (July) 1943.

Although standards for judging the nutritional status of children are as yet incomplete, such methods as are available have demonstrated the relation of nutrition to diet and of diet to economic status, agricultural resources and education. The war, with its great shifts of population and demand on transportation, has produced temporary difficulties in the availability of food. Also, the employment of mothers may easily interfere with the provision of adequate food for children. In this connection the importance of school lunches is increased. The laws requiring enrichment of bread with iron salts, thiamine, nicotinic acid and dried milk may be expected to be beneficial. In the rationing of food special study is given to the needs of mothers and children. With proper distribution the supply of food is at present adequate.

LESLIE, Evanston, Ill.

THE PROBLEM OF NUTRITION IN PERU: ITS PRESENT CONDITION IN REGARD TO THE DIFFERENT PERIODS OF CHILDHOOD. MANUEL SALCEDO FERNANDINI, *Bol. Inst. internac. am. de protec. a la infancia* **17**:111 (July) 1943.

Adequate nutrition for expectant mothers is the first step toward nutritional protection of future children.

Breast feeding should be widely encouraged (by providing lunchrooms for nursing mothers, subsidizing breast feeding and establishing stations for the dispensing of breast milk) as a means by which to secure and protect the health of preschool children.

School lunchrooms should be established in areas where children have to travel long distances to attend school.

FROM THE EDITOR'S SUMMARY.

Vitamins; Avitaminoses

THE RATIO OF ASCORBIC ACID, RIBOFLAVIN AND THIAMINE IN RAW AND PASTEURIZED MILK. ARTHUR D. HOLMES, CARLETON P. JONES, ANNE W. WERTZ and JOHN W. KUZMESKI, *J. Nutrition* **26**:337 (Oct.) 1943.

The ascorbic acid content of raw milk averaged 19.7 ± 0.18 mg. per liter and of pasteurized milk $15.9 \pm$

2.7 mg. per liter. The riboflavin content of raw milk averaged 1.51 ± 0.09 mg. per liter and of pasteurized milk 1.48 ± 0.01 mg. per liter. The thiamine content averaged 0.33 ± 0.02 mg. per liter in raw milk and 0.30 ± 0.03 mg. per liter in pasteurized milk. The ratios to each other of riboflavin, ascorbic acid and thiamine were computed for both the raw and the pasteurized milk.

FREDEEN, Kansas City, Mo.

A CASE OF VITAMIN D DEFICIENCY ASSOCIATED WITH CIRRHOSIS OF THE LIVER AND A DYSCRASIA OF CALCIUM AND PHOSPHORUS METABOLISM. H. F. FRASER, J. Pediat. **23**:410 (Oct.) 1943.

The author reports the case of a boy 18 years of age with a history of intrauterine exposure to chronic illness of the mother and with a diet definitely deficient in minerals and vitamins during the first years of life. There was advanced clinical rickets at 2 years of age associated with a moderate enlargement of the liver. No specific therapy was given until the child was 9 years old, when he was sent to the country for the summer and a great improvement in walking ability followed extensive exposure to sunshine.

At 18 years of age metabolic studies showed a dyscrasia in calcium and phosphorus metabolism which may be described as follows. There was a relatively constant urinary or endogenous excretion of calcium irrespective of the intake. The normal person with an intake of 0.4 Gm. excretes only about one fourth of the ingested calcium via the kidneys and the remainder in the feces; the patient reversed this ratio and excreted more calcium in the urine than in the feces.

In general, the balances for phosphorus were like those for calcium, with two chief differences: The derangement of the mechanism was even greater; a larger proportion of the phosphorus was excreted via the kidneys. Except during the two periods of low ingestion of phosphorus the patient maintained a positive phosphorus balance, whereas with a normal intake of calcium there was a negative balance.

Death occurred at 19 years from pulmonary tuberculosis. Necropsy observations which were pertinent showed that the dentin of the teeth was riddled with interglobular spaces and that the enamel was hypoplastic. The bones showed a definite thinning of the cortex, and the red marrow was hyperplastic. The two parathyroid glands which were isolated were normal, grossly and histologically. The liver displayed advanced portal cirrhosis.

FRASER, Bethesda, Md.

AN EVALUATION OF THE BLOOD AND URINARY THIAMINE DETERMINATIONS IN VITAMIN B₁ SUBNUTRITION. REUEL A. BENSON, C. MICHAEL WITZBERGE and LAWRENCE B. SLOBCDY, J. Pediat. **23**:437 (Oct.) 1943.

Subnutrition in respect to vitamin B₁ does not present definite signs and symptoms and can be detected, at present, only by laboratory procedures. In a study on "healthy" children who were hospitalized and so could be closely observed, children with sufficient thiamine for tissue saturation fulfilled three criteria: (1) a daily intake of more than 900 micrograms (300 U. S. P. units) of thiamine and a thiamine-calory ratio of 400 micrograms per thousand calories; (2) an average of 150 micrograms or more of thiamine excreted daily in the urine, and (3) a urinary excretion of 20 per cent or more of the ingested thiamine.

The urinary excretion of thiamine of 75 ill children was then studied. Many of these children did not meet

the foregoing criteria and presented varying degrees of unsaturation of the tissues with thiamine. A search the causes of this unsaturation usually revealed an adequate dietary intake of thiamine, an impaired absorption, or an increased demand due to increased metabolism.

Test doses, which may be valuable in verifying actual clinical states of deficiency or marked unsaturation of the tissues, gave variable and inconsistent results in children with slight tissue unsaturation (vitamin subnutrition).

A study was made of the levels of vitamin B₁ in blood in patients with varying degrees of saturation and unsaturation of the tissues with thiamine.

One hundred and sixty-six children could be divided into four groups on the basis of studies of urinary excretion of thiamine. Group 1 consisted of 100 children who met the three criteria of saturation of the tissues with thiamine. The levels of blood thiamine in this group varied from 4.8 to 13.7 micrograms per hundred centimeters, with a mean of 8.0 ± 1.1 . Group 2 consisted of 29 children who were on the borderline regarding their vitamin B₁ nutrition. The levels of blood thiamine varied from 5.2 to 12.4 micrograms, with mean of 8.3 ± 1.0 . Group 3 consisted of 15 children whose levels of blood thiamine were definitely below normal, from 4.5 to 10.7 micrograms per hundred centimeters, with a mean of 8.0 ± 1.3 .

Thus in spite of unequivocal evidence of unsaturation of the tissues with thiamine as shown by the urinary excretion studies, the levels of vitamin B₁ in the blood were within the same range as those of the group of normal children. The conclusion was drawn that determinations of the amount of vitamin B₁ in the blood were useless for the detection of vitamin B₁ subnutritional states, that is, of unsaturation of the tissues with thiamine without clinical signs or definite symptoms. It seemed reasonable, however, to expect the level of vitamin B₁ in the blood to fall in instances of severe clinical thiamine deficiency, and this has been shown to occur. The amount of vitamin B₁ held in the blood apparently does not fall until the stores of the vitamin in the tissues are almost exhausted.

BENSON, New York.

EFFECT OF CECECTOMY AND SUCCINYL-SULFATHIAZOLE ON VITAMIN K SYNTHESIS. K. G. WAKIM, MER M. KRIDER and HARRY G. DAY, Proc. Soc. Exptl. Biol. & Med. **54**:164 (Oct.) 1943.

Young rats raised on a diet deficient in vitamin K were subjected to cecectomy and two days after operation were given succinylsulfathiazole. Of the 17 animals studied severe hypoprothrombinemia developed in 1 and within three months nearly all had died from hemorrhage. If given 2-methyl-1,4-naphthoquinone, the prothrombin time returned to normal. Of 9 animals similarly fed and operated on but not given the succinylsulfathiazole, 7 showed a normal prothrombin time and 2 showed only a slight increase. Animals not operated on but given succinylsulfathiazole showed only a slight increase in the prothrombin time.

HANSEN, Minneapolis.

Hygiene; Growth and Nutrition; Public Health

MATERNAL MORTALITY IN PARAGUAY. RICARDO ODRIO SOLA, Bol. Inst. internac. am. de protec. a la infancia **16**:253 (Oct.) 1942.

The author at the beginning of his work praises the fortitude of Paraguayan women.

The statistical report from 1908 to 1917 shows that 2 per cent of the infants born were girls and that 9 per cent of the total deaths occurred in girls and men, that is, fewer girls were born while the number deaths among women was higher than among men. From 1920 to 1940, 5,607 women died, 13.3 per cent in diseases due to pregnancy, from childbirth or from causes subsequent to childbirth. Forty-six and three-tenths per cent of these deaths were due to puerperal sepsis; 15.4 per cent to other puerperal affections, 1.2 per cent to albuminuria and eclampsia, 4.6 per cent to puerperal tetanus and 1.2 per cent to embolism. Of 300 mothers from 15 to 50 years of age, 300 might have been saved.

The author believes that the way to avoid this causality is by improving the rural environment, by changing the present hut into a comfortable home. He proposes the establishment in each settlement of special schools to teach such subjects as child care, domestic science and care of the sick. The people of the working classes should be taught the advantages of adequate nutrition; in this task the agencies of primary education and public health should cooperate. Finally the author emphasizes the importance of extending services for protection of mothers and children and points out the necessity of establishing maternity clinics and clinics for emergencies in areas where there are no hospitals.

FROM THE EDITOR'S SUMMARY.

ORGANIZATION OF THE SERVICES OF NUTRITION FOR SCHOOL CHILDREN. PERLINA WINOCUR, Rev. de hig. y med. Escolar. **2:85**, 1943.

The Department of Elementary School Health of the National Council of Education in Argentina fulfills a broad function by compensating in one way or another the deficient nutrition of school children. It provides them either with a daily glass of milk or with a full meal at school canteens. These benefits are also received by weak, undernourished children attending open air schools and summer camps.

The department carries out an educational program effectively in the clinic of nutrition.

FROM THE AUTHOR'S SUMMARY.

Prematurity and Congenital Deformities

CONGENITAL MALFORMATIONS INDUCED IN RATS BY MATERNAL NUTRITIONAL DEFICIENCY: V. EFFECTS OF A PURIFIED DIET LACKING RIBOFLAVIN. JOSEF WARKANY and ELIZABETH SCHRAFFENBERGER, Proc. Soc. Exper. Biol. & Med. **54:92** (Oct.) 1943.

From previous work (Warkany and Nelson: *Science* **62:383**, 1940) it was found that congenital malformations developed in the offspring of female rats fed on a low cornmeal, wheat gluten, calcium carbonate and sodium chloride plus vitamin D and that these abnormalities could be prevented by supplementing the maternal diet with 2 per cent dried pig liver. In these studies a different diet consisting of sucrose, casein, vegetable oil and salt mixed with various vitamin supplements save riboflavin was fed to 21 female rats of the Sprague-Dawley strain, mated to normal males of the same strain which were on adequate diets, with the production of 74 young rats. Ten of these newborn animals showed abnormalities of the type which the former diet produced. These malformations consisted of shortness of the mandible, tibia, fibula, radius and

ulna, fusion of the ribs, sternal centers of ossification, syndactylism, brachydactylism and cleft palate.

HANSEN, Minneapolis.

Newborn

THE COMPARATIVE EFFECTS OF AMMONIATED MERCURY, SULFATHIAZOLE, AND SOAP AND WATER ON THE SURFACE BACTERIA OF THE NEWBORN INFANT. WALTER R. MACLAREN, J. Pediat. **23:446** (Oct.) 1943.

The subjects of this study were 42 healthy newborn infants. Each received a careful cleansing with soap and water within twelve hours after birth. Thirteen of the infants were then given one generalized application of 2.5 per cent ammoniated mercury ointment and on each succeeding day received only a light bath with sterile cottonseed oil. Fourteen of the infants were given one generalized application of 7.5 per cent sulfathiazole ointment and similar cottonseed oil baths. Fifteen were given no applications of ointment but were given a bath with soap and water on alternate days and were rubbed with cottonseed oil each day. The ointments used were prepared with a petrolatum and hydrous wool fat base.

Cultures were made of material taken from the skin of all infants at twenty-four hour intervals during the first five days of life by means of a wire loop dipped in sterile broth. The cultures were grown on blood agar.

For the five days following a single application of either drug there was a much slower rate of increase of bacteria on the skin than was found with the use of soap and water alone. The effect of the two drugs was approximately the same.

Staphylococcus albus, *staphylococcus aureus* and beta hemolytic streptococci were, in the order named, the organisms most commonly isolated. Fewer beta hemolytic streptococci were found after the use of sulfathiazole.

No absorption of the drug or cutaneous irritation was demonstrated from the use of sulfathiazole, which suggests that it is preferable to ammoniated mercury or soap and water alone in the care of the skin of the newborn infant.

MACLAREN, Los Angeles.

PHYSIOLOGY OF THE HEMATOPOIETIC SYSTEM IN INFANTS AND YOUNG CHILDREN, INCLUDING THE BLOOD PICTURE AT BIRTH AND IN YOUNG INFANTS. PEARL LEE, J. Pediat. **23:676** (Dec.) 1943.

The newborn infant begins life with a blood picture peculiar to the age group, characterized by an increase in number of most of the cellular elements and the presence of a few immature cells. Rapid changes, caused mostly by physiologic factors, take place during the first few weeks, greatly reducing the hemoglobin content and the number of red cells. After three months slow recovery begins.

FROM THE AUTHOR'S SUMMARY.

THE PATHOGENESIS OF FETAL ERYTHROBLASTOSIS. PHILIP LEVINE, New York State J. Med. **42:1928** (Oct. 15) 1942.

Three forms of fetal erythroblastosis are recognized: congenital hydrops, icterus gravis and anemia of the newborn. Some women have all except, perhaps, their first infants so affected. Recent studies on the causes of accidents resulting from intragroup transfusions have resulted in the discovery that immunization of the

mother by one or more blood factors present in the fetus but not in the mother is responsible for these accidents and also for fetal erythroblastosis. The obstetric histories of these mothers show abortions, miscarriages, stillbirths, neonatal deaths and cases of toxemia. Isoimmunization of the mother by blood factors in the fetus occurs; then the maternal immune agglutinins penetrate the placenta and act on the susceptible fetal blood.

The Rh factor, which is inherited as a simple mendelian dominant, is transmitted from the father to the fetus and immunizes the mother with Rh-negative blood. The anti-Rh agglutinins are best demonstrated in the mother's blood soon after the delivery of an infant with erythroblastosis; even then in not more than 50 per cent of the cases can it be detected. The discovery that the father's blood is Rh positive and the mother's Rh negative establishes the diagnosis for a child in whom this condition is suspected. This is especially helpful in borderline cases. A mother with Rh-negative blood artificially inseminated with serum from a male with Rh-negative blood should have a normal child. In order to prevent accidents in transfusions donors with Rh-negative blood should, of course, be selected for patients with such blood.

An increased incidence of congenital malformations in infants with erythroblastosis has been reported. Other conditions, such as abortions, miscarriages, stillbirths, neonatal deaths, eclampsia, icterus neonatorum and icterus gravis, may be due to factors yet to be discovered. "Incompatibility of the blood groups of the mother and fetus may possibly play a role in inducing either early or late fetal death."

AIKMAN, Rochester, N. Y.

Acute Contagious Diseases

INTRADERMAL TEST FOR SUSCEPTIBILITY TO AND IMMUNIZATION AGAINST WHOOPING COUGH USING AGGLUTINOGEN FROM PHASE I HAEMOPHILUS PERTUSSIS. EARL W. FLOSDORF, HARRIET M. FELTON, A. BONDI and AIMS C. MCGUINNESS, *Am. J. M. Sc.* **206**:421 (Oct.) 1943.

From a study of 650 children with known histories of pertussis it appears that the purified agglutino-gen of *Haemophilus pertussis* should provide an excellent reagent for assisting in control of whooping cough.

Classification of immune and susceptible persons on the basis of the cutaneous test with purified pertussis agglutino-gen agrees with classification according to the histories of incidence of infection and vaccination with *H. pertussis*. The test procedure can also be used as a means of stimulation of immunity following primary vaccination. In persons having an existing immunity to pertussis at the time of the test an increase is produced in the agglutination titer. In persons with no initial immunity, repeated test doses will produce a reversal of the reaction and a measurable agglutination titer. The reagent gives promise of value at the time of epidemics, not only to determine persons who are susceptible but to increase the degree of immunity in persons having but a partial immunity to pertussis.

HENSEE, Omaha.

THE TREATMENT OF MENINGOCOCCUS CARRIERS WITH SULFADIAZINE. F. S. CHEEVER, B. B. BREESE and H. C. UPHAM, *Ann. Int. Med.* **19**:662 (Oct.) 1943.

A total of 8 Gm. of sulfadiazine administered during a period of seventy-two hours was found to be effective

in clearing the nasopharynx of meningococci in adults. No untoward effects were noted.

READING, Galveston, Texas.

EXPERIMENTAL INVESTIGATION OF MEASLES. GEOFFREY RAKE, *J. Pediat.* **23**:376 (Oct.) 1943.

The virus of measles has been cultivated in tissue culture and on the chorioallantois or in the amniotic allantoic cavities of the developing chick embryo. Chorioallantoic cultivation has been most frequently used, and in twenty-seven attempts seventeen strains have been established. One of these has been carried through one hundred and twenty passages during more than seventeen months.

The egg passage material has been inoculated in children by subcutaneous, intradermal and intranasal routes, the last by means of either a drip or a fine nebulized spray. Mild measles has been produced in the majority of children, particularly by intradermal injection or intranasal spray. The types of measles seen can be divided into moderate, mild or minimal, and even in the moderately severe cases malaise and cough are absent or very slight. Of 839 children inoculated and followed carefully, 450, or 54 per cent, have shown definite signs of measles.

This mild "measles inoculata" can be passed by contact to susceptible persons, and the severity of the disease is not enhanced by such passage. There are as yet insufficient data as to the degree of protection against the natural disease afforded by vaccination.

RAKE, New Brunswick, N. J.

PROTECTION OF THE INFANT AGAINST DIPHTHERIA DURING THE FIRST YEAR OF LIFE FOLLOWING THE ACTIVE IMMUNIZATION OF THE PREGNANT MOTHER. J. LIEBLING and H. E. SCHMITZ, *J. Pediat.* **23**:43 (Oct.) 1943.

The purpose of this publication is to present the effect of actively immunizing pregnant women and to relate the effect of this immunization on the infant during the first year of life.

Diphtheria antitoxin titers were determined on both the mothers and the infants at six weeks and three months after the birth of the infants. Antitoxin titers were ascertained by the Moss-Jones modification method and the Schick tests were done in the usual manner.

The results showed that active immunization of the pregnant mothers produced an increased placental transfer of passive immune bodies to the offspring.

The newborn infants of these actively immunized mothers gave negative reactions to the Schick test at birth and in some these reactions remained negative at 7 and 13 months of age; others showed a positive reaction from 9 months to 1 year of age. However the increased transfer of passive immune bodies to the offspring is prolonged sufficiently to increase the protection during the first year of life.

Schick tests on pregnant mothers immune to diphtheria acted as a secondary antigenic stimulus, causing increased antitoxin formation. This stimulus was sufficient to prolong the passive immunity in the infant of this group of mothers. The Schick tests on infant immune to diphtheria did not increase the antitoxin titers.

The authors conclude that the transplacental transfer of the immune bodies to the offspring is sufficient to protect the infant during the first year of life and that a Schick test performed as a routine procedure on the pregnant mother would have a twofold purpose

) It would demonstrate and separate the immune others from those not immune and (b) at the same time serve as a secondary stimulus to the mothers who have negative reactions to the test. Those who showed positive reaction would require active immunization.

SCHMITZ, Chicago.

PEDICULAR PARALYSIS: ITS DESCRIPTION AND TREATMENT. ELIZABETH KENNY, New Orleans M. & S. J. **96:134** (Oct.) 1943.

The author stresses her view that the disorders of muscular physiology which occur in poliomyelitis are (1) muscle spasm, (2) mental alienation and (3) muscle incoordination. The method of care is discussed, and the reasons for failure of the treatment are pointed out.

BERKLEY, Beverly Hills, Calif.

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES, Pub. Health Rep. **58:1625** (Oct. 29) 1943.

For the period of Sept. 12 to Oct. 9, 1943, the incidence of poliomyelitis was the highest reported in the United States since 1931. The epidemic appeared in all sections of the country except the South Atlantic and East South Central. The incidence of meningitis was increased in all sections. The number of cases of measles was the highest for this period in the last ten years, and the incidence of scarlet fever was 1 per cent above the median. The total death rate from disease was 5.2 per cent above the median.

SANFORD, Chicago.

DIPHTHERIA IN THE MIDDLE EAST. T. A. MACGIBBON, Edinburgh M. J. **50:617** (Oct.) 1943.

While serving in a tented hospital in Egypt, the author observed 71 cases of diphtheria in adults, 52 of which were proved by laboratory studies. Forty-nine were faucial and pharyngeal. There were also nasal and nonrespiratory complications, namely, wounds, desert sores, burns and cutaneous lesions. The frequency of complications of diphtheria despite antitoxin therapy was unusual even for an adult group. Complications were most frequent in the faucial type. Laryngitis and myocarditis were the most common complications, being nearly equal in frequency. Paresis was usually of the descending type. The myocarditis was severe enough to be the cause of death in 3 cases. The author discusses the symptoms of the latter complication. The difficulty of diagnosing the least common diphtheria lesions and the failure of adequate treatment with antitoxin to prevent complications which extend the average period of hospitalization from sixty to one hundred and thirty-one days provoked him to urge active immunization of all military personnel.

NEFF, Kansas City, Mo.

THE SCHICK TEST IN YOUNG ADULTS. N. E. GOLDSWORTHY and H. WILSON, M. J. Australia **2:349** (Oct. 30) 1943.

Forty-six per cent of 109 nurses and 50 per cent of 26 university undergraduates reacted positively to the Schick test. The proportion of reactors was higher than would be expected from statements in some standard textbooks. This discrepancy is probably explained by the effect of environment—social status, size of community, density of population. The problem of immunity to diphtheria is discussed with respect to (1)

immunity as shown by the Schick test, (2) antitoxic immunity and (3) clinically effective immunity.

GONCE, Madison, Wis.

Acute Infectious Diseases

THE TREATMENT OF DYSENTERY CARRIERS WITH SUCCINYL-SULFATHIAZOLE: OBSERVATIONS ON THE MINIMAL EFFECTIVE DOSE. PAUL S. BARKER, Am. J. Digest. Dis. **10:443** (Dec.) 1943.

Succinylsulfathiazole was given to three dysentery carriers in amounts of 0.147, 0.195 and 0.220 Gm. per kilogram of body weight daily. These amounts did not successfully eliminate the dysentery bacilli from the stools when given for seven days, but when given for fourteen days they were effective. A fourth patient did not respond to 0.166 Gm. of the drug per kilogram daily for fourteen days but was rendered free from dysentery bacilli by the administration of 0.25 Gm. per kilogram daily for five days. A fifth patient recovered spontaneously from the carrier state.

Although relatively small amounts of succinylsulfathiazole are effective if administration is continued for a long time, it would seem more practical to give at least 0.25 Gm. per kilogram daily for five to seven days. This amount should uniformly eliminate dysentery bacilli from the stools of carriers in a short time.

MORRISON, Savannah, Ga.

SALICYLATE THERAPY IN RHEUMATIC FEVER: A RATIONAL TECHNIQUE. ALVIN F. COBURN, Bull. Johns Hopkins Hosp. **73:435** (Dec.) 1943.

The author believes that infection is an essential component of the rheumatic reaction and is not modified by salicylate therapy. So long as the infection is active, the patient is subject to inflammatory reactions in the heart and in the vascular tissues throughout the body. The author's observations indicate that the inflammatory reaction may be suppressed and the development of the stigmas of heart disease may be prevented by the administration of large doses of sodium salicylate (10 Gm. daily).

The article is too long to abstract completely; it should be read by all persons interested in this subject.

LYTTLE, New York.

ON THE ANAPHYLACTIC NATURE OF RHEUMATIC PNEUMONITIS. ARNOLD R. RICH and JOHN E. GREGORY, Bull. Johns Hopkins Hosp. **73:465** (Dec.) 1943.

In preceding papers we have shown that cardiac and arterial lesions having the basic characteristics of those of acute rheumatic fever can be produced experimentally as a result of anaphylactic hypersensitivity. The present comparison of the peculiar lesion of rheumatic pneumonitis with that of pneumonitis caused by hypersensitivity to the sulfonamide drugs shows that the two are basically identical and that both exhibit the primary damage to the capillaries which is characteristic of focal anaphylactic reactions. This similarity provides additional evidence in support of the view that the lesions of acute rheumatic fever may be anaphylactic in origin.

FROM THE AUTHORS' SUMMARY.

REPELLANTS IN MALARIA CONTROL. S. ANNECKE, South African M. J. **17:383** (Dec. 25) 1943.

As a repellent to *Anopheles gambiae* and *Anopheles funestus*, which are largely responsible for the natural

transmission of malaria in the whole Ethiopian region, oil of citronella, plain or fortified, is superior to oil of Tagetes and to a cream containing powdered pyrethrum and naphthalene.

GONCE, Madison, Wis.

Chronic Infectious Diseases

PRIMARY TUBERCULOSIS COMPLICATED BY BRONCHIAL TUBERCULOSIS WITH ATELECTASIS (EPITUBERCULOSIS). EDNA M. JONES, T. N. RAFFERTY and H. S. WILLIS, *Am. Rev. Tuberc.* 46:392 (Oct.) 1942.

Tuberculosis in children develops in a variety of ways. In the majority there is a relatively uneventful recovery to the condition known as the end picture of the primary complex. In some patients extrapulmonary disease develops. Some have an irregular course in which tuberculous pneumonia or extensive pulmonary tuberculosis is diagnosed. Among the latter is a rather large group whose main disorder is not tuberculosis but pulmonary atelectasis, heretofore classified as epituberculosis. Among 716 children admitted to the sanatorium, roentgenograms of 85, or 12 per cent, showed the homogeneous shadow of so-called epituberculosis. Bronchoscopic examinations were made on 42 of these children, and 31 were found to have bronchial distortion or disease, chiefly narrowing of the lumen by pressure from enlarged lymph nodes at the root or by a tuberculoma or an ulcer. The obstruction produced may develop slowly or rapidly, continuously or intermittently. The general condition produced by these factors is also variable and may not show the so-called classic signs of atelectasis such as an elevated diaphragm, narrowed interspaces or a shifted mediastinum. The end result of any such obstruction is a functionless lobe, which may be shrunken and without air, normal or increased in size, or may have fluid replacing the air.

The term epituberculosis is no longer needed and should be abandoned.

EUGENE SMITH, Ogden, Utah.

PHYSICO-CHEMICAL PROPERTIES OF THE ARSPHENAMINES IN RELATION TO DISTRIBUTION AND RETENTION IN THE TISSUES. F. B. RODMAN and HAROLD N. WRIGHT, *J. Pharmacol. & Exper. Therap.* 79:140 (Oct.) 1943.

Arsphenamine and neoarsphenamine can be separated into colloidal and crystalline fractions. In view of the marked difference in both therapeutic and toxic properties of the crystalloid and the colloid fractions of the arsphenamine, it appeared desirable to investigate possible differences in the affinity for and the storage in tissues of these separated fractions, since these might have an important bearing on the question of cumulative poisoning. The authors, therefore, investigated this subject in rats (308), making 3,400 separate analyses. The excellent paper is too long and detailed for simple abstraction, but the conclusions (in greater part) follow:

1. The colloid fraction of both arsphenamine and neoarsphenamine is the portion of these drugs which is retained for the longest time. It penetrates into the tissues readily, as is shown by the sharp rise in arsenic in the tissues in the early time periods, and it also appears to be relatively firmly held by the tissues, since it is reexcreted slowly into the blood stream. The arsenic which is returned by the tissues to the blood stream is in turn eliminated from the animal body only with considerable difficulty, since a considerable portion of the injected colloid fraction was found to be still

present in the blood stream at the end of thirty day. The greater part of the colloid fraction was found in the blood and the liver, but the skin, the muscles, the bones and the intestinal tract also took up large percentages of the injected colloid fraction. All the tissues examined showed retention of the colloid fraction for a longer period than was shown by either the whole drug or the crystalloid fraction.

2. The crystalloid fraction showed a high degree of initial penetration of the drug into the tissues with subsequent rapid lowering of their concentration of arsenic. The excretion of the crystalloid fraction from the tissues is much faster than that of either the whole drug or the colloid fraction.

3. The whole drug occupies an intermediate position but with a decided tendency to follow more closely the greater and more prolonged retention pattern of the colloid fraction.

4. The distinctive affinity of arsphenamine for the liver and of neoarsphenamine for the kidney has been confirmed and elaborated.

5. When injected into rats in equivalent doses neoarsphenamine is retained by practically all tissue (except the blood and those of the gastrointestinal tract) to a greater extent than arsphenamine, regardless of its physicochemical characteristics.

PILCHER, Cleveland.

USE OF BACTERIAL ASPHYXIA FOR HOMOLOGOUS ANTIGEN PRODUCTION IN EXPERIMENTAL IMMUNIZATION AGAINST HUMAN-TYPE TUBERCULOSIS. TRUMAN SQUIRE POTTER, *Proc. Soc. Exper. Biol. & Med.* 54:143 (Oct.) 1943.

The growth removed from 10 one month old glyceric agar cultures of human tubercle bacilli was placed in Pyrex glass tubes with a small amount of water and sealed under a vacuum to remove oxygen. Death of the bacilli was proved by culture and animal inoculation. A total of 33 rabbits was immunized by six weekly subcutaneous injections of approximately 13 mg of the asphyxiated vaccine. Four months later these rabbits together with a similar number of control animals were inoculated intravenously with virulent tubercle bacilli. Four and 3 animals of each group respectively, inoculated within three to six months, died of nontuberculous causes. After eight to ten months the animals were killed in pairs and examined grossly and microscopically. Twenty-four of the immunized rabbits showed no lesions of tuberculosis, whereas 22 of the control animals showed evidence of tuberculosis. The authors state the belief that parasitic asphyxia is a new principle to be used in the study of immunity and should be tried for study on human and avian tuberculosis.

HANSEN, Minneapolis.

TUBERCULIN INDEX IN PUBLIC SCHOOL CHILDREN. JOAQUIN ENRIQUE HERRAN, *Rev. de hig. y med. escolar.* 2:7, 1943.

The tuberculin index was studied in 953 school children chosen by the district medical inspectors to go to summer camps supported by the National Board of Education of Argentina. The schools attended by the children are situated in the twelve districts that include the greatest part of the federal district exclusive of the suburban area. A tuberculin index of 37.78 per cent was found for a group of children with an average age of 9.05 years.

The financial conditions of the children's homes were classified, as good when the income allowed 35 pesos or

ore for each member of the family; as fair when it allowed from 25 to 35 pesos per person, and as bad when it allowed less than 25 pesos per person. It was found that the families of 14.79 per cent of the children were in good, 18.78 per cent in fair and 66.42 per cent in bad financial condition.

For children averaging 9 years of age the tuberculin index was 41.81 per cent for those attending school canteens supported by the National Board of Education, and 30.10 per cent for those attending open air schools supported by the National Board of Education. The similarity between the tuberculin indexes for groups of children attending school canteens and those chosen to go to summer camps may be due to similarity in the social environment even though they belong to zones of the city which do not exactly coincide.

FROM THE AUTHOR'S SUMMARY.

Diseases of Blood, Heart and Blood Vessels and Spleen

THE MECHANISM OF AURICULAR PAROXYSMAL TACHYCARDIA. P. S. BARKER, F. N. WILSON and F. D. JOHNSTON, *Am. Heart J.* **26**:435 (Oct.) 1943.

Evidence is brought forth to show that auricular paroxysmal tachycardia is caused by circus rhythm which involves either the sinoauricular or the auriculo-ventricular node.

GIBSON, Chicago.

A STUDY OF HEMOGLOBIN METABOLISM AND HEMATOLOGY IN A CASE OF CONGENITAL HEMOLYTIC JAUNDICE DURING (A) CLINICAL CRISIS, (B) REPEATED TRANSFUSIONS, AND (C) BEFORE AND AFTER SPLENECTOMY. ROBERT C. LOWE, *Am. J. M. Sc.* **206**:347 (Sept.) 1943.

A case of congenital hemolytic jaundice is presented in which the chemistry of the blood and the excretion of pigment were studied during the course of a crisis and during repeated transfusions and after splenectomy.

During the crisis certain observations indicated a decrease in hepatic function which cleared spontaneously. There was no evidence of severe destruction of blood cells. These changes have been observed also in crises of sickle cell anemia. The observations suggest the theory that hepatic disease may be a factor in the crises of such attacks. Transfusions were followed by a progressive enlargement of the spleen. There then occurred an increase in destruction of blood cells and a decrease in the number of erythrocytes and reticulocytes and in the amount of hemoglobin. It is probable that the transfused red cells were sequestered in the spleen and rapidly destroyed, leading to the high excretion of stercobilin.

Splenectomy was followed by a return to normal in the number of red blood cells, the amount of hemoglobin, the percentage of reticulocytes and the excretion of pigment. The bilirubinemia and all clinical symptoms and signs disappeared.

HENSKE, Omaha.

CONGENITAL HEART BLOCK: A STUDY OF TWO CASES IN HEALTHY ADULTS. THOMAS C. JALESKI and EUGENE T. MORRISON, *Am. J. M. Sc.* **206**:449 (Oct.) 1943.

The authors report 2 cases of congenital heart block. The first patient, who had been studied for four years, was a healthy adult with no cardiac symptoms and no

other apparent anomalies. The second patient, whose condition had been followed from birth, had had no cardiac symptoms except for some syncopal attacks. This patient's case is of particular interest in that she has had two normal pregnancies without any disturbing symptoms.

HENSKE, Omaha.

INFLUENCE OF ALIMENTATION ON THE REGENERATION OF PLASMA PROTEINS FOLLOWING A SINGLE SEVERE NONFATAL HEMORRHAGE. CARL E. LISCHER, ROBERT ELMAN and HARRIET W. DAVEY, *Am. J. Physiol.* **139**:638 (Aug.) 1943.

The authors conclude that the presence or absence of exogenous sources of protein or carbohydrate does not influence the rapidity with which the body compensates for the acute loss of plasma protein during the first seventy-two hours after a single severe nonfatal hemorrhage.

NOURSE, Cleveland.

THE EARLY RADIOLOGIC RECOGNITION OF MITRAL VALVE DISEASE. BERNARD S. EPSTEIN, *J. Pediat.* **23**:381 (Oct.) 1943.

The earliest cardiac enlargement due to mitral valve disease which can be seen roentgenologically is an enlargement of the left auricle. This is best identified by examining the patient fluoroscopically in the right anterior oblique position after administering a bolus of barium sulfate. Posterior deviation in the course of the esophagus in the region of the left auricle is of diagnostic significance. This change may occur when the heart presents a normal frontal silhouette and has been found more reliable than measurements made from the teleroentgenograms and tables of patients' heights and weights. Roentgenologic examinations of the heart should be made with this in mind. A diagnosis of a functional murmur should not be made if there is definite roentgenologic evidence of left auricular enlargement.

EPSTEIN, Brooklyn.

EXPERIENCES WITH THE RH SUBSTANCE IN TRANSFUSION REACTIONS. R. W. KOUCKY, *Minnesota Med.* **26**:980 (Nov.) 1943.

The author warns us that the new data concerning the Rh substance should be received with enthusiasm but at the same time should not obscure the many lessons previously learned regarding the successful management of blood transfusions. After reviewing the records of 16 cases and checking his observations with those found in a large number of references he concludes that the Rh substance is in general similar to the A and B substances which determine the division of blood into its four groups. Persons with Rh-positive blood cannot become sensitized. In mothers with Rh-negative blood antibodies may develop from the fetus during pregnancy or after transfusion. The Rh substance varies greatly in its antigenic property; some people become sensitized very readily, while others either form no antibodies or do so only to a slight degree. The antibody which can be demonstrated in the laboratory is the agglutinin. Apparently other types of antibodies are formed which are not detected by laboratory tests but will produce transfusion reactions or erythroblastosis in the fetus. The absence of demonstrable agglutinins, therefore, does not exclude the presence of other dangerous antibodies.

STOESSER, Minneapolis.

HAEMOLYTIC ANAEMIAS. L. J. DAVIS, Edinburgh M. J. 50:589 (Oct.) 1943.

The author gives a survey of recent views on hemolytic anemias. After defining the anemias and the mechanism of cell destruction, he outlines the methods of investigation. In addition to careful history, physical examination and usual laboratory studies on peripheral blood and sternal marrow, he stresses a careful recording of such a manifestation as fecal urobilinogen, which would point to intracellular destruction. Hemoglobinuria would indicate intravascular hemolysis. Therapeutically these are important, as pointed out by Haden; splenectomy would not be expected to be of benefit if the pathologic condition is due to intravascular destruction, unless it is assumed that the diffusible lytic agent may emanate from the spleen.

He classifies the anemias according to their known or supposed cause: (1) abnormality of the red cells; (2) hemolysis; (3) parasitic infection of red cells; (4) poisons exerting lytic or other action on red cells; (5) hypersensitivity to drugs or other agents; (6) unknown cause associated with known predisposing factors, and (7) cause completely unknown. He proceeds then to discuss the pathologic picture of each with particular reference to the mechanism of destruction. His description of familial acholuric jaundice, erythroblastosis fetalis and lead poisoning will be of interest to the pediatrician, as will his discussion of nocturnal hemoglobinuria, of anemia associated with burns and neoplastic disease and of acute hemolytic anemia of unknown cause.

NEFF, Kansas City, Mo.

THROMBOCYTOPENIC PURPURA. HORACE EVANS and KENNETH M. A. PERRY, *Lancet* 2:410 (Oct. 2) 1943.

Of 75 patients with thrombopenic purpura treated at the London Hospital between 1927 and 1933, 30 had not reached puberty. They were equally divided between the sexes. Ten patients recovered spontaneously; splenectomy was successful in the treatment of 5 boys and unsuccessful in the treatment of 4 girls. The mortality during the period of observation was 16 per cent.

Other forms of treatment that were used without apparent benefit were the administration of vitamins C, K and P.

LANGMANN, New York.

A FATAL BLOOD TRANSFUSION REACTION APPARENTLY DUE TO THE RH FACTOR. N. C. NEWTON and A. H. TEBBUTT, *M. J. Australia* 2:109 (Aug. 7) 1943.

The authors report the case of a woman aged 48 who had had four normal children and one miscarriage at the sixth week of pregnancy and who was admitted to the hospital for treatment of uterine hemorrhage of thirteen weeks' duration. The first blood transfusion produced a severe reaction; and a second transfusion, given ten days later, was fatal. The woman's red cells were Rh negative, and her blood serum contained anti-Rh agglutinins in a titer of 1 in 8. Unfortunately, Rh determinations were not made on blood of the husband or the donors, but, on the basis of incidence, it is assumed that their blood was Rh positive.

GONCE, Madison, Wis.

A PRELIMINARY NOTE ON THE RELATIONSHIP OF TO BLOOD PLATELETS TO THE MECHANISM OF HAEMOSTASIS. G. REID, *M. J. Australia* 2:244 (Sept. 2) 1943.

A vasoconstrictor substance liberated when the blood platelets break down plays a part in checking hemorrhage from arterioles and larger vessels. The name "thrombocytin" is suggested for this substance. There is no evidence in the literature nor could the author demonstrate that the vasoconstrictor substance derived from platelets causes capillary constriction.

Patients suffering from thrombopenic purpura with prolonged bleeding times and reduced numbers of platelets yielded serum possessing only feeble vasoconstrictive activity (the test object being an isolated spiral strip of carotid artery from an ox).

The blood platelets of a patient suffering from non-thrombopenic purpura did not differ from normal platelets with respect to the liberation of "thrombocytin."

GONCE, Madison, Wis.

Diseases of Nose, Throat and Ear

FACTORS INFLUENCING THE DURATION OF ACUTE TONSILLITIS. M. TAMARI and ALEX M. BERMAN, *Illinois M. J.* 84:269 (Oct.) 1943.

In the analysis of a large number of cases of acute tonsillitis at the Illinois Charitable Eye and Ear Infirmary, it was found that changes of season not only increased the number of cases but prolonged the duration of acute tonsillitis and increased the number of complications.

Other conditions which decrease the general resistance of the person and prolong the duration of acute tonsillitis are rickets, anemias, tuberculosis and other debilitating diseases. Streptococci and pneumococci are mostly responsible for acute tonsillar infections. Local conditions extending an attack of acute tonsillitis are chronic infections of the teeth and the mouth, chronic sinusitis and chronic infections of the larynx, the trachea and the bronchi.

Swabbing, painting and washing in the crypts, as well as section of the tonsils during acute attacks, are mechanical therapeutic efforts which retard the normal healing process. Infections of stumps or larger tonsillar remains are marked by more painful and more prolonged duration. Another factor influencing the normal course of acute tonsillitis is incomplete radium or roentgen therapy.

BARBOUR, Peoria, Ill.

TREATMENT OF VINCENT'S ANGINA OF THE TONSIL. C. S. LINTON, *J. A. M. A.* 123:341 (Oct. 9) 1943.

Linton briefly comments on the therapy of Vincent's angina with particular reference to the cases encountered in the armed forces. In addition to his discussion he presents a few case reports.

Of all the methods of treatment the following have been adopted as the simplest and most practical: A 0.5 Gm. sulfathiazole tablet is dissolved on the tongue every two hours during the day and a 1 Gm. tablet dissolved on the tongue every four hours during the night; this plan is to be continued for two days, a

nich time the patient will either discontinue it voluntarily because symptoms have disappeared or continue a little longer if necessary. If infection is present so about the gum margins, it is advised that the lfathiazole tablet be moistened with a few drops of ater to make a paste and this rubbed into the gum argins.

GORDON, Philadelphia. [ARCH. OTOLARYNG.]

REVENTION OF EAR AND NASAL SINUS COMPLICATIONS OF THE COMMON COLD. DAVID A. DOLOWITZ, W. E. LOCH, H. L. HAINES, A. T. WARD JR. and K. L. PICKRELL, J. A. M. A. **123**:534 (Oct 30) 1943.

These authors discuss in moderate detail the bacteriology of the common cold with particular emphasis on the pyogenic organisms responsible for the complications that so often occur in the ears and the nasal accessory sinuses.

Their method of investigation consisted of a bacteriologic and clinical study of patients arranged in groups, one group being treated by the technic soon to be outlined, another being used as a control and a third not participating in the experiment but reporting to the infirmary with complications of the common cold. Each patient was carefully examined daily with transillumination, with a nasal speculum, especial emphasis being placed on pus or secretions under the anterior ends of the middle turbinate, and with a nasopharyngoscope. Material from the nose, the nasopharynx and the pharynx was cultured before treatment was begun and daily thereafter until the patient was discharged.

The primary object of the treatment was not to cure common colds, for they were probably initiated by a virus infection, but to prevent the bacterial infections of the sinuses, the ears and the pharynx that so commonly follow colds.

The treatment consisted of spraying the nose and the pharynx with a 2.5 per cent solution of sulfadiazine in ethanalamine solution, the control group receiving the solvent alone; those not participating in the experiment were managed by the usual empiric methods.

Bacteriologic studies show that the sulfadiazine spray does not sterilize the nose and the throat with the occasional exception of beta hemolytic streptococcus infection. Many patients with a red, edematous pharynx and constitutional symptoms due to streptococcal infection are cured within twenty-four hours both bacteriologically and clinically by using only 20 to 25 cc. of the 2.5 per cent sulfadiazine solution as a spray. In order to get this result it is imperative that the treatment begin as soon as possible after the sore throat is noticed, and while the bacteria are still on the surface. The results are not so good if the treatment is begun after the fourth day of the disease. Other strains of streptococci and pneumococci do not disappear or noticeably diminish in numbers in the cultures, but the clinical results suggest that they lose their virulence or their ability to become virulent.

Extension of infection to the sinuses, the ears or the larynx is rare in properly treated patients.

Sensitivity to these medicaments was discussed, though it was not observed in this series of experiments.

The authors, modest in their conclusions, infer that this subject should be given further consideration by medical investigators.

GORDON, Philadelphia. [ARCH. OTOLARYNG.]

SINUSITIS AND INFECTIONS SECONDARY TO THE COMMON COLD. F. M. TURNBULL, W. E. HAMILTON, E. SIMON and M. F. GEORGE JR., J. A. M. A. **123**:536 (Oct. 30) 1943.

After the work of Turnbull, who reported that use of a 5 per cent solution of the sodium salt of sulfathiazole brought relief from the symptoms of chronic sinusitis, the authors set out to investigate further. They found that this solution was unstable when exposed to light and air and that crystallization and discoloration were the rule.

They added sodium sulfite and found that the solution was then stable to air, light and heat. A vasoconstrictor, dl-desoxyephedrine hydrochloride (discovered by Ogata in 1919 and like the original sulfanilamide a "sleeper" for twenty years), was found compatible with sodium sulfathiazole and actually formed a new sulfonamide drug, desoxyephedronium sulfathiazole.

Synergism developed so that only a small portion of the vasoconstrictive agent was necessary to achieve the hoped-for results.

Packs saturated with the substance were placed in the acutely swollen membranes of the nasal cavity and kept in situ for twenty to thirty minutes.

The clinical studies were applied over a wide range and in cases of acute, especially severe, disease, in which the mucosa was engorged. The patient was placed in the modified Proetz position and was given at five minute intervals instillations of 10 to 15 drops of this solution until the congestion of the tissues was sufficiently reduced to give relief from pressure.

Home treatment consisted of instillations of drops or sprayings at five minute intervals, usually two or three, until the deeper tissues of the nose were reached.

Acute pharyngitis and laryngitis were treated by spraying the nose and the throat and, in office treatments, the larynx and the upper part of the trachea.

Acute suppurative otitis media was treated by myringotomy and insertion of medicated tampons in patients treated in the office and by drops in the ear, the nose and the epipharynx when the treatment was given by the patient at home.

Chronic suppurative otitis media was treated by instillation of drops of solution of hydrogen peroxide followed by insertion of tampons; home treatment consisted in the prescribed use of drops.

All of these measures were found safe and effective.

The authors emphasize that the methods outlined are not to be considered a cure-all, nor can they supplant indicated surgical treatment.

GORDON, Philadelphia. [ARCH. OTOLARYNG.]

WORKING WITH SPEECH DEFECTIVES IN PUBLIC SCHOOLS. HILDRED SCHUELL, J. Speech Disorders **8**:355 (Dec.) 1943.

The author discusses the methods by which children with various defects in speech, such as stuttering, delayed speech and the defects due to cleft palate, are handled in the public schools with the assistance of the school nurse and the school psychologist.

PALMER, Wichita, Kan.

PREVENTION AND TREATMENT OF ACOUSTIC TRAUMA. GEORGE E. SHAMBAUGH JR., J. Speech Disorders **8**:369 (Dec.) 1943.

The most common type of loss of hearing observed after acoustic trauma is a decrease in sensitivity to sounds with a frequency of approximately 4,096, and

the next most frequent type is complete loss of hearing. Temporary or permanent damage to the nerve cells in the inner ear always occurs.

Prevention is essential since there is no treatment for acoustic trauma. The following preventive measures are suggested: 1. Routine audiometric testing should be done on all persons, such as aviators, who are exposed to excessively loud noises. 2. Persons susceptible to acoustic trauma should be transferred to quieter surroundings. 3. Excessive noise should be controlled by the use of improved designs for engines, machinery and buildings. 4. Where noise cannot be reduced, aural protectors should be worn. The most important preventive measure is repeated routine audiometric testing.

PALMER, Wichita, Kan.

A SECOND STUDY IN THE AFFECTIVE VALUE OF SPEECH SOUNDS. JON EISENSEN, JEROME FISHER and SYLVIA G. SUCHER, *Quart. J. Speech* **29**:457 (Dec.) 1943.

In this study 69 deaf subjects, of whom 34 had congenital defects in hearing but had been taught oral speech, were questioned as to whether they considered certain speech sounds pleasant or unpleasant. Both persons with normal hearing (from a previous experiment) and deaf persons reacted to most isolated speech sounds as being pleasant. Both normal and deaf persons agreed that "z," "j," "th," hard "g," "zh" and "wh" are unpleasant sounds.

PALMER, Wichita, Kan.

A PREDISPOSING CAUSE OF STUTTERING. JOHN M. FLETCHER, *Quart. J. Speech* **29**:480 (Dec.) 1943.

An important predisposing cause of asynergic movements, such as those observed in stuttering, is the fact that a person has only indirect control over the muscles involved in such movements, since the asynergies disappear when the remotely controlled muscles are eliminated.

PALMER, Wichita, Kan.

CONGENITAL CYST OF THE LARYNX. JANE I. DAVIDSON, *Lancet* **2**:508 (Oct. 23) 1943.

Congenital cysts of the larynx are rare. They may manifest themselves at birth or give rise to no symptoms until adult life. Those which cause symptoms at birth are commonly fatal if not promptly recognized. Cure by simple aspiration has been reported. The diagnosis can be made by laryngoscopy or by palpation.

Only 15 cases of the condition in infants have been reported.

A case is reported in which the patient, an infant, died on the twenty-fourth day of life. At autopsy a cystic swelling about 5 mm. in diameter was found on the left wall of the larynx, almost completely occluding the orifice.

LANGMANN, New York.

Diseases of Lungs, Pleura and Mediastinum

THE ISOLATION AND IDENTIFICATION OF PATHOGENIC FUNGI FROM SPUTUM. JOSEPH M. KURUNG, *Am. Rev. Tuberc.* **46**:365 (Oct.) 1942.

The foreword by Harry A. Bray best describes the manual which is incorporated in this number of the *American Review of Tuberculosis*.

"Diseases of the lung due to infection by fungi have been regarded as extremely rare. Recent studies, however, have disclosed that such infections are not uncommon and that the pulmonary lesions encountered are as varied in nature as those in tuberculosis. The

diagnosis usually is established by the recovery of the offending fungus from the sputum. Their identification may prove a formidable task to those not familiar with the subject. The terminology and classification is difficult to master and the morphology and cultural characteristics vary widely.

"The manual presents the essential laboratory procedures and the conditions required for optimal cultivation of the pathogenic fungi found in the sputum. The age of the culture and the magnification adopted for the microscopical study are exactly stated, an important feature. The appearance of the colony and the microscopical details are liberally illustrated. It would seem that the information contained in the manual should suffice for the identification of the offending fungus in the sputum."

EUGENE SMITH, Ogden, Utah.

CHRONIC ASPIRATIVE BRONCHOPNEUMONIA IN YOUNG INFANTS. A. CASTELLANOS, RAÚL PEREIRAS, R. VALDÉS DÍAZ and B. SÁNCHEZ SANTIAGO, *Arch. de med. inf.* **12**:191 (Oct.-Dec.) 1943.

This interesting article is profusely illustrated with roentgenograms and with photomicrographs of tissues from the lung of 2 infants with chronic pneumonic processes due to aspiration of milk. The authors differentiate the condition from pulmonary steatosis due to a disturbance of lipid metabolism. In both instances there was no initial acute asphyxia, no oily laxatives had been used, the patient had not received intranasal instillations of cod liver oil. The roentgenograms of the infants were distinctive, but the final diagnoses were made from pneumograms taken after the introduction of air through capillary punctures. Chemical investigation showed that the cells did not contain liquid petrolatum or cod liver oil; the lipid was derived from milk. The authors wish to emphasize the importance of capillary puncture as a means of diagnosis of obscure pulmonary conditions.

SANFORD, Chicago.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

HEPATIC DAMAGE ASSOCIATED WITH SULFONAMIDE THERAPY IN INFANTS AND CHILDREN: I. MORPHOLOGIC PATHOLOGY. MAUDE L. MENTEN and MARIE A. ANDERSCH, *Ann. Int. Med.* **19**:609 (Oct.) 1943.

Thirty-eight of a total of 299 necropsies performed on children who had been treated with sulfonamide compounds showed hepatic disease. Toxic necrosis of the liver was found in 3 cases, toxic central necrosis in 9 cases and serous hepatitis with early central necrosis in 26 cases.

There appeared to be no relationship between the types or severity of the hepatic disease and the amount of the sulfonamide drug or drugs administered.

READING, Galveston, Texas.

HEPATIC DAMAGE ASSOCIATED WITH SULFONAMIDE THERAPY IN INFANTS AND CHILDREN. II. CHANGES IN LIVER FUNCTION TESTS. MARIE A. ANDERSCH, *Ann. Int. Med.* **19**:622 (Oct.) 1943.

Gray's test of hepatic function was used in a study of 106 patients. The serums of 73 of these children were tested periodically during treatment with sulfonamide drugs, and single determinations were made for the serums of the remaining 33. Twenty-four of the 73

showed varying degrees of positive reactions to the drugs; 49 showed no change in reaction during therapy.

READING, Gal-eston, Texas.

PEPTIC ULCERS IN INFANCY AND CHILDHOOD. MIRIAM C. BENNER, J. Pediat. 23:463 (Oct.) 1943.

The author reports postmortem studies of children from 2 days to 11 years of age, 7 of whom had duodenal and 1 of whom had gastric ulcers. Two of the children were newborn infants. One of the cases was unusual in that there was a history of gastrointestinal symptoms though the infant was only 3 days of age. The other case of ulcer in an infant was remarkable in that severe inflammation was present in the ulcer, a rare condition in an age period when ulcers are thought to be due almost exclusively to vascular accidents at the time of birth. In 2 cases ulcers were found in association with severe infectious disease of the central nervous system. In 1 of these the appearance of the ulcer indicated that it was of the chronic type and that it antedated the onset of the disease of the nervous system. Two cases in which only scars of previous ulcers were present are included in the report to emphasize the possibility of ulcers occurring without symptoms and healing without specific treatment. Only 1 child had lesions of the gastric mucosa, and in this instance the ulcers were superficial and probably terminal. One case is of interest because of the association of ulcer with possible poisoning by rhubarb leaves.

BENNER, Denver.

JAUNDICE AND CONDITIONS ASSOCIATED WITH THIS PHENOMENON. MADELEINE FALLON, J. Pediat. 23:721 (Dec.) 1943.

Jaundice in newborn and older infants and in children is classified on the basis of destruction of blood, obstruction in the liver or in the biliary passages and destruction of hepatic tissue.

Icterus neonatorum, infectious jaundice, anomalies of the bile ducts, erythroblastosis and familial jaundice are discussed, and the difficulties encountered in the differential diagnosis are illustrated with histories of cases.

It is believed that the Rh factor sets the stage for erythroblastosis but that it is not the sole cause. Familial jaundice is classified as mild, moderate and severe. In cases of severe and sometimes of moderate familial jaundice splenectomy must be done early to produce a cure. The article is illustrated with roentgenograms showing the skeletal changes which occur in familial jaundice.

FALLON Los Angeles.

Nervous Diseases

GROWTH ASYMMETRY DUE TO LESIONS OF THE POST-CENTRAL CEREBRAL CORTEX. WILDER PENFIELD and J. S. M. ROBERTSON, Arch. Neurol. & Psychiat. 50: 405 (Oct.) 1943.

From a study of the exposed brains of patients with focal epilepsy, the authors describe pathologic changes in the central nervous system associated with asymmetry of growth. They conclude that the latter condition is caused by failure of growth on one side rather than hypertrophy of the other side and that this failure in growth is due to cortical injury (evidenced by scars). In patients with bodily asymmetry the lesions were in

the region of the central fissure, and they had occurred by the time the patient was 2 years of age.

BEVERLY, Chicago.

BLOOD-SUCKING VECTORS OF ENCEPHALITIS: EXPERIMENTAL TRANSMISSION OF ST. LOUIS ENCEPHALITIS (HUBBARD STRAIN) TO WHITE SWISS MICE BY THE AMERICAN DOG TICK, DERMACENTOR VARIABILIS SAY. RUSSELL J. BLATTNER and FLORENCE M. HEYS, J. Pediat. 23:371 (Oct.) 1943.

Since the epidemic of acute encephalitis in the St. Louis area which occurred in the summer of 1933 and recurred in the summer of 1937, the mode of transmission of St. Louis encephalitis has been of special interest. While the general consensus has seemed to favor droplet infection, certain features of this disease suggest the possibility of a blood-sucking vector. These features are discussed.

Experiments are described which give evidence that the common dog tick, Dermacentor variabilis Say, is capable of being infected by the virus of St. Louis encephalitis through feeding on inoculated animals and, once infected, can transmit the virus to normal susceptible animals by bite. Further, a female can transmit the infection to her offspring through the egg, and the infection may persist through all stages of metamorphosis into the second generation. A tick once infected remains infected for at least four months. Thus far the virus of St. Louis encephalitis has not been recovered from ticks collected in nature, but no extensive studies of this problem have been undertaken.

It is not the opinion of the authors that the dog tick is the natural vector responsible for the transmission of St. Louis encephalitis virus to man. No history of tick bite has been obtained in any case of St. Louis encephalitis observed. However, it is possible that the tick may play a role in the natural epidemiology of the disease by maintaining the virus as an endemic focus in lower animals and that the virus may be carried to human beings by another blood-sucking vector, such as the mosquito, possibly Culex tarsalis, as the work of Hammon suggests. The present work is of theoretic significance, since it represents the first successful transmission of the virus of St. Louis encephalitis to experimental animals by a blood-sucking vector.

BLATTNER, St. Louis.

THE EFFECT OF HEAD INJURY ON HEARING. W. E. GROVE, J. Speech Disorders 8:363 (Dec.) 1943.

Lesions resulting in defective hearing are restricted to the eighth nerve or the cochlear contents. Examination for hearing is not reliable in the early days after injury due to the disturbed condition of the sensorium. Repeated examinations are necessary in each case, for medical or legal purposes, for the detection of malingering. A history of the case should be elicited. Two hundred and eleven cases of proved fracture of the skull were studied, and 49 cases of fracture involving the base of the skull. There was perceptive deafness in 45 cases. In unilateral, longitudinal fracture, the function of hearing is more damaged as age increases. The perceptive type of deafness is most common. The ear on the side of the fracture sometimes shows a greater loss of hearing than its fellow, but in a large number of instances the loss is the same in both ears. In 65 per cent of the cases of bilateral longitudinal fracture there was loss in perceptive hearing. Labyrinthine fracture produced total deafness on the affected side in every instance and some loss on the opposite side in most

instances. One person had a complete loss of hearing as a result of labyrinthine fracture. Patients may regain a great deal of hearing even a month after an accident. If deterioration of hearing does not occur in the first six months, the condition will probably remain stationary.

The author discusses the methods recommended by the American Medical Association for evaluating loss of hearing. These methods probably will not be useful in evaluating the amount of loss suffered by men in the armed forces because of the method in which hearing is tested at the time of induction.

PALMER, Wichita, Kan.

Psychology and Psychiatry

INFLUENCES OF WAR AS EVIDENCED IN CHILDREN'S PLAY. ELEANOR PALMER BONTE AND MARY MUSGROVE. *Child Development* 14:179 (Dec.) 1943.

The influences of war as evidenced in children's play were studied in eleven kindergarten and two church preschool groups in Honolulu, Territory of Hawaii, by means of direct observation, analysis of teacher's responses to questionnaires and analysis of children's paintings. The data were analyzed with reference to: (1) the manifestations of the influences of war in various activities of play; (2) the extent to which war play takes place and the proportion of children participating; (3) the degree of participation in war play in relation to sex, race and domestic background; (4) the initiating, terminating and overstimulating circumstances of war play, and (5) participation in war play in relation to social, emotional and psychologic factors. The interpretation stresses war play as merely another normal manifestation of the effects of environmental stimuli which retains all the values of normal play, which has no deleterious effect on social and emotional development and which even contributes to the development of some positive characteristics of personality. The authors conclude that there is no justifiable reason for suppressing war play and that with guidance by teachers positive educational values can be fostered.

FROM THE AUTHORS' SUMMARY.

THE EFFECTS OF EARLY INSTITUTIONAL CARE ON ADOLESCENT PERSONALITY (GRAPHIC RORSCHACH DATA). W. GOLDFARB, *Child Development* 14:213 (Dec.) 1943.

This is a report of one phase of an experimental and observational investigation of 15 adolescents whose rearing during the first three years of life had been in an institution for infants and whose subsequent experience was in foster homes (institution group). These children were contrasted with an equated group of 15 children whose major experience had been with foster families and whose total experience had been with families (foster home group).

The children reared in institutions showed a greater deviation from the "normal" graphic Rorschach pattern than did the children from foster homes. The deviation manifested itself in unusual adherence to the "concrete" attitude and in inadequate conceptualization. The "concreteness" is specifically represented in such qualities as apathy in relation to environment and behavior that is unreflective, unaccountable and without conscious purpose. Thus the graphic Rorschach data tend to confirm the observations and conclusions based on other investigative devices which also showed that the children from institutions are clearly differentiated from those

from foster homes. The characteristics of children from institutions inferred from the mass of data are (1) an impoverished, undifferentiated personality, with deficiency in inhibition and control, and (2) passivity or apathy of personality.

FROM THE AUTHOR'S SUMMARY.

PSYCHIATRIC PROBLEMS IN ADOLESCENCE. DAVID SLIGHT, *Illinois M. J.* 84:255 (Oct.) 1943.

Since the emotional reactions and habits are still fluid and have not yet crystallized, the adolescent has no acquired the more or less irreversible commitments of life which so often complicate treatment of the neurotic adult. Thus, since the patterns are still flexible, the prospects are better for alterations and readjustment of unhealthy habits and attitudes.

Among the most severe psychiatric disorders, schizophrenia is most common, and relatively few other types are seen in early adolescence. More often than is believed, trends of a psychotic nature are present during adolescence but are overlooked or misunderstood. Adolescence brings new problems in the mental deficiencies, because of the new and increasing social demands, the development of sexual conflicts and so on.

Symptoms of the neuroses, such as obsessions and phobias, are common in adolescence. These symptoms are often concealed by the adolescent or appear in forms that are misunderstood. They are often treated without recognition of the fact that they are due to emotional conflict.

Most of the psychiatric disorders of adolescence occur in general forms and are manifest as seclusiveness, undue indulgence in fantasies, disobedience to parents and teachers and irregular habits. There has been a recent increase in offenses against persons, which are more serious than those offenses against property.

The most fruitful concept in psychopathology is that of conflict. The aim of education and training is to develop a compromise or a balance whereby the person can function physically, mentally and socially to the best advantage.

In the present generation there has been a remarkable disharmony in the process of social development. Thus, because of the laudable advances in pediatrics, maternal hygiene and other health efforts adolescents show a remarkable development in physique, with physical maturity at an earlier age than in previous generations. There have been an extension of the period of school attendance and a raising of the age of going to work. In many cases there has been a resultant delay in the development of social maturity. This disharmony should be kept in mind in considering the nature and the occurrence of psychiatric problems of the adolescent of the time.

The development toward maturity may become fixed. Then the adolescent fails to accept or acquire disciplined reactions and socially mature habits in keeping with his age. He may not only fail to progress; he may regress. Failure to solve the various conflicts may result in mental symptoms or in visceral incoordination.

In the diagnosis of the general disorders it must be determined whether the emotional difficulties are of a transient and passing nature or indicate a deeper conflict and whether they are due to external causes or to basic difficulties in the development of personality. The most important point to establish in diagnosis is

the capacity of the adolescent to face and overcome the rebuffs and the frustrations of life.

In treatment it must be remembered that the difficulties of the child are often due to external circumstances which can be altered. Some of the patterns of life are being crystallized within, and to that extent a change within is necessary. For young adolescents changes in parental attitudes and other factors in the social situations as well as changes in the reactions of the patient must be attempted.

Some adults are still prone to rebuff adolescents who want to talk about their emotional difficulties instead of adopting attitudes that would make it easy for them to reveal their intimate and personal difficulties. Group measures of prevention and treatment should be developed. A change in the public attitude toward psychiatric disorders is needed. This militates against acknowledgment of their presence or of the need for treatment in the early stages.

Good results are often possible in the minor psychiatric disorders with a few interviews on a friendly and an objective basis that permits ventilation of the persons' difficulties. Many require only a sympathetic understanding to get a new perspective. Their social contacts and experiences should be established and enlarged through group activities of all kinds.

In some patients the factor of constitutional hypersensitivity may loom large in the causal process. These persons require more time than their fellows to adopt new ways and to relinquish present habits and attitudes.

BARBOUR, Peoria, Ill.

Diseases of the Genitourinary Tract

THE IMPORTANCE TO THE ADOLESCENT GIRL OF GYNECOLOGICAL EXAMINATIONS. EDWARD ALLEN, Illinois M. J. **84**:251 (Oct.) 1943.

Allen states the belief that many of the cases of primary amenorrhea, oligomenorrhea, adolescent menorrhagia, essential dysmenorrhea, congenital erosions or malformation, and infantilism will someday be avoided by further study and earlier treatment of the adolescent girl. Proper, early education of the child in the psychology and the physiology of sex will prevent many illegitimate or unwanted pregnancies, with their consequent criminal abortions and accompanying pelvic infections. Further advances in endocrine and nutritional therapy will aid greatly in the care of those patients who have been educated to come regularly for attention.

Pelvic examination of the adolescent girl should be progressive. For an infant, careful inspection is usually sufficient. Such inspection included in each subsequent physical examination will lead the child to accept readily the more extensive palpatory and instrumental prepubertal examination indicated before the onset of the menstrual flow. Subsequent examinations during the period of adolescence will obviate entirely those last minute premarital examinations which all too frequently and far too late uncover gross pathologic conditions or malformations.

BARBOUR, Peoria, Ill.

TREATMENT OF CRYPTORCHIDISM. FLOYD E. HARDING, J. Pediat. **23**:451 (Oct.) 1943.

Cryptorchidism without mechanical obstruction may be corrected with hormonal therapy. That the administration of chorionic gonadotropin caused descent of the testes in the cases reported was beyond doubt. There was a question as to whether the addition of

pituitary gonadotropin increased the incidence of descent. Testosterone when added produced further enlargement of the parts, and this was an indication for its use. The testicles descended in 76 per cent of the 38 patients treated in this series. Since the number of patients with obstruction varies and it is usually impossible to diagnose which patients have obstruction, the prognosis varies. With endocrine treatment, obstruction can be diagnosed early so that the necessary surgical procedures can be performed not later than the prepuberty period; thus one prevents the atrophy that occurs in the testicles which is allowed to go through puberty undescended. Certain mental and physical conditions make it advisable to treat some of these boys at a younger age. The boys so treated became more muscular, played better, became broader through the shoulders, gained in height and were generally considered "more boy" in type. The problem children took orders, cooperated and developed a more mature attitude. There were increased dependability and fulfillment of necessary tasks with better grades at school. When descent does not follow treatment, orchidopexy must be used to prevent sterility, hypogonadism, complications and possibly the development of a malignant growth. Operation should be facilitated by the previous use of a treatment that induces lengthening of the spermatic cord and enlargement of the scrotum and testicle. In the cases reported no harm to the testicles could be detected, regardless of the age at which the boy was treated.

HARDING, Los Angeles.

OVARIAN CYST. J. F. MORANO BRANDI, Rev. Soc. pédiat. de la Plâta **4**:109 (Dec.) 1943.

A girl 12 years old had pain in the hypogastrium. A tumor could at times be palpated. At operation a cyst of the right ovary was found and removed. The pedicle of the ovary was unusually long, more than 15 cm. There was no gangrene or other complication.

HIGGINS, Boston.

Diseases of the Ductless Glands; Endocrinology

THE PRODUCTION OF HYPOTHALAMIC OBESITY IN RATS ALREADY DISPLAYING CHRONIC HYPOPITUITARISM. A. W. HETHERINGTON, Am. J. Physiol. **140**:89 (Oct.) 1943.

Ten rats hypophysectomized and observed for about eleven weeks showed no signs of obesity. Some, even after so long a time, had not attained their preoperative weight; others had surpassed it by a few grams only. They could be considered, therefore, to be in a state of chronic hypophysial insufficiency. Hypothalamic lesions were then produced in these animals by the Horsley-Clarke technic. Within three to four weeks they began to display rapid deposition of fat and eleven weeks after the second operation they were definitely obese. This evidence shows that the fat depots are still able to store excess fat in response to hypothalamic damage after they have suffered the changes in tissue metabolism presumed to be attendant on hypophysectomy. Since neither total nor partial hypophysectomy produces adiposity or prevents its appearance after hypothalamic damage is done, it is not likely that the hypophysis is involved in the production of obesity often associated with injury to structures in the pituitary region. Hypothalamic disorder appears to be the sole responsible factor.

NOURSE, Cleveland.

INACTIVATION OF ESTRONE AND DIETHYLSTILBESTROL BY MICROORGANISMS. BERNHARD ZONDEK and FELIX SULMAN, *Endocrinology* **33**:204 (Oct.) 1943.

It has been shown that estrone is inactivated in the liver and the spleen in warm blooded animals, in the body in cold-blooded animals, and in plants. Aqueous solutions of estrone kept for two months in the laboratory undergo a considerable loss of potency.

It appeared possible that micro-organisms which decompose estrone and diethylstilbestrol might be widespread, and it therefore seemed of interest to study the decomposition of these substances by various micro-organisms.

Of 32 nonpathogenic and 29 pathogenic strains of micro-organisms tested 2 of the former and none of the latter produced inactivation of estrone. The titer of a solution of estrone was tripled by contact with yeast.

JACOBSEN, Buffalo.

THE INTRASPLENIC INJECTION OF ESTROGENS AND THEIR ESTERS. ALBERT SEGALOFF, *Endocrinology* **33**:209 (Oct.) 1943.

Evidence has been gradually accumulating from diverse lines of investigation which would indicate that the liver is the site of extensive inactivation of estrogen. The author reports a series of experiments on rats, involving intrasplenic injection of estrogens, in which an attempt was made to quantitate the role of the liver in the process of inactivation.

JACOBSEN, Buffalo.

CONSTANCY OF ANDROGEN CONCENTRATION IN THE URINE. FRANKLIN HOLLANDER, BRUNO KREISS, EMANUEL KLEMPNER and ROBERT T. FRAN, *Endocrinology* **33**:217 (Oct.) 1943.

It has been generally believed that the quantity of androgenic substances excreted in the urine is independent of the urinary volume.

In 9 human subjects studied over a period of a month the concentration of biologically active androgens in the urine was constant and independent of the daily urinary output, even with forced and restricted fluid intakes. The total output of androgen per twenty-four hours showed considerable variation.

So far as is known, no other urinary constituent is present in a constant concentration independent of the volume of fluid excreted.

JACOBSEN, Buffalo.

INHIBITING EFFECT OF ADRENOCORTICOTROPIC HORMONE ON THE GROWTH OF MALE RATS. HERBERT M. EVANS, MIRIAM E. SIMPSON and CHOH HAO LI, *Endocrinology* **33**:237 (Oct.) 1943.

The authors conclude that the body growth of normal and gonadectomized male rats is inhibited by pure adrenocorticotrophic hormone from sheep. The inhibition does not occur in adrenalectomized rats.

JACOBSEN, Buffalo.

INACTIVATION OF STILBESTROL BY LIVER IN VITRO. BERNHARD ZONDEK, FELIX SULMAN and JOACHIM SKLOW, *Endocrinology* **33**:333 (Dec.) 1943.

Diethylstilbestrol is inactivated by liver pulp in vitro but less rapidly than is estrone. It is suggested that this fact explains the greater oral efficiency and the toxic side effects of diethylstilbestrol in man.

JACOBSEN, Buffalo.

REPRODUCTIVE CAPACITY IN ADULT MALE RAT TREATED PREPUBERALLY WITH ANDROGENIC HORMONE. JAMES G. WILSON and HARRIET C. WILSON, *Endocrinology* **33**:353 (Dec.) 1943.

Male rats given injections of testosterone propionate showed defects in the structure and function of the reproductive organs.

JACOBSEN, Buffalo.

RESISTANCE OF RATS TO POTASSIUM POISONING AFTER ADMINISTRATION OF THYROID OR OF DESOXYCORTICOSTERONE ACETATE. BERTRAND E. LOWENSTEIN and RAYMUND L. ZWEMER, *Endocrinology* **33**:361 (Dec.) 1943.

Desoxycorticosterone acetate protected the normal rat from poisoning due to potassium chloride and induced physiologic atrophy of the adrenal cortex. Feeding of thyroid increased the toxicity of potassium chloride in the normal rat and resulted in compensatory physiologic hypertrophy of the adrenal cortex.

JACOBSEN, Buffalo.

TROPIC VERSUS-TROPHIC IN THE TERMINOLOGY OF THE PITUITARY HORMONES. GEORGE W. CORNER, *Endocrinology* **33**:405 (Dec.) 1943.

Corner gives clear evidence that the use of such terms as adrenotropic and thyrotropic is contrary to a well established prior use of the suffix in biologic terminology and actually reverses the cause and effect relationship intended. The suffix "trophic" seems more appropriate.

JACOBSEN, Buffalo.

STUDIES IN HORMONE THERAPY: I. THE EVALUATION OF GROWTH HORMONE THERAPY. ALFRED A. STRAUSS and ERNEST H. WATSON, *J. Pediat.* **23**:421 (Oct.) 1943.

Standard tables of weight, height and other measurements of growth, admittedly inadequate for appraisal of apparently normal children, are entirely unsuitable as guides in studies of growth-retarded children. Recourse was therefore made to the age unit method of Olson to evaluate the effects of treatment with anterior pituitary extracts rich in the growth hormone on such children. Olson portrays data on growth (measurements of height in inches, weight in pounds) by translating them into common age units. Thus weight is recorded as weight age and height as height age by simply comparing the crude measurement (pounds, inches) with Olson's tables. (Olson, W. C., and Hughes, B. O.: *Tables for the Translation of Physical Measurements Into Age Units*, Ann Arbor, Michigan, The University of Michigan Press, 1938.) This method has the advantage of rendering understandable and usable data on growth collected in various types of units. Chronologic age for each patient is, of course, a straight line, irrespective of the form of the curve of original measurements. Against the patient's chronologic age line are graphed his weight age, height age, dental age and mental age. Deflections of these several curves immediately reveal periods of retardation, acceleration or arrest.

The growth of 4 children during six to eight years, including pretreatment, treatment and post-treatment periods, is recorded by the above method. Judged by the usual methods of appraisal the response to anterior pituitary growth hormone was disappointing, but when graphically portrayed by Olson's age unit method a favorable modification of the growth curves was evident. Such a modification is all that can be expected, and

he use of standard tables for appraisal of such modification is highly unsatisfactory.

This article includes a discussion of two additional methods of employing the age unit method to record growth and to appraise modifiers of growth. One of these makes use of the height ratio (height quotient).

WATSON, Ann Arbor, Mich.

OSTEODYSTROPHIA FIBROSA CYSTICA [OSTEITIS FIBROSA CYSTICA] AND JUVENILE HYPERTHYROIDISM. J. E. JACOBS, South. M. J. **36**:668 (Oct.) 1943.

The author reports 2 cases of juvenile hyperthyroidism in which there was osteitis fibrosa cystica with diffuse osteoporosis complicated by pathologic fractures. One patient is well three years after thyroidectomy. The other child, who has had no operative treatment, is still toxic, showing osteoporosis and pathologic fractures from time to time. Calcium and phosphorus metabolism in thyrotoxicosis are briefly discussed, and a differential diagnosis is offered.

SCHLUTZ, Chicago.

Diseases of the Muscles, Bones, Joints and Lymph Glands

DETERMINATION OF BONE AGE IN CHILDREN. LOUIS A. LURIE, SOL LEVY and MAX L. LURIE, J. Pediat. **23**:131 (Aug.) 1943.

The authors describe a simple but accurate and inexpensive method for determining skeletal age of children. In this study the roentgenograms of various centers of ossification of 2,100 white children ranging in age from 2½ to 19 years were examined. Of this number the records of only 1,129 children (704 boys and 425 girls) were used, the remainder being excluded because the children were suffering from either endocrine disorders or severe nutritional disturbances. Four roentgenograms were made in each case, the hand including the wrist, the elbow, the pelvis and the foot including the ankle.

Each child's roentgenograms were read from the standpoint of the time of appearance of the various centers of ossification as well as the time of their fusion. The results were tabulated on the basis of one year differences in age. Since girls show an accelerated skeletal maturation, separate charts were made for boys and girls.

The authors epitomize their data in two charts which portray graphically the degree of maturation of the various centers of ossification (epiphyses) which is present at any given age. From these charts, the physician can determine at a glance which epiphyses should be present, which are likely to be present and which are only infrequently present or fused at a given age. Conversely, the physician can quickly determine the skeletal age of his patient by comparing the actual conditions as shown on the films with the data on the charts.

A new term, bone quotient (B.Q.) is introduced. This is determined by dividing the skeletal age by the chronologic age. The resulting figure represents the percentage of normal maturation of the bones which has occurred. The bone quotient is of further value in diagnosing certain metabolic and endocrine disorders and also in furnishing a uniform basis for statistical studies and analyses.

SONTAG, Yellow Springs, Ohio.

THE EFFECT OF ILLNESS AND OTHER FACTORS ON THE APPEARANCE PATTERN OF SKELETAL EPIPHYSES. LESTER WARREN SONTAG and JANET LIPFORD, J. Pediat. **23**:391 (Oct.) 1943.

By converting the time of first appearance of centers of ossification as determined from regularly spaced roentgen examinations of the skeletons of the same children to Z scores, it is possible to compare the sequence of appearance of one child's centers with those of others. Each center of each child was compared with the yearly Z score mean of that child, and a center deviating from that mean by .6 sigma or more was designated as "aberrant." Monozygotic twins have the same centers aberrant significantly more often than siblings. Siblings have the same centers aberrant more often than randomly selected nonsiblings. The correlation coefficient for the Z scores of monozygotic twins was 0.82, for siblings 0.32 and for nonsiblings 0.06. There is evidence, therefore, of a genetic factor in sequence of appearance of centers of ossification.

The children with the most "aberrant" centers had had no more acute illnesses during the first six years of life than had the children with the least "aberrant" centers. Children with the most illness had no more aberrant centers than those with the least illness. There was no evidence, therefore, that acute illness tended to delay those centers about to appear at the time the illness occurred. Children with most acute illness had a more rapid appearance of centers than did those with least illness, although their order was not changed. The rate of appearance of centers of ossification in skeletal epiphyses varies tremendously from year to year in many children.

SONTAG, Yellow Springs, Ohio.

CONGENITAL SACROCOCCYGEAL TUMORS: CASE REPORT OF A TERATOMA. M. P. NEAL and J. B. CARLISLE, South. M. J. **36**:677 (Oct.) 1943.

The authors report a case of congenital sacrococcygeal teratoma with other anomalies and malformations, multiple fractures and partial dismemberment incident to delivery. The case confirms the statement, commonly made, that when one developmental defect occurs others are to be expected.

SCHLUTZ, Chicago.

AN EPIDEMIC OF POLYARTHRITIS IN THE NORTHERN TERRITORY. J. H. HALLIDAY and J. P. HORAN, M. J. Australia **2**:293 (Oct. 9) 1943.

The authors report an epidemic among soldiers of an acute febrile disease of unknown causation, characterized by a fleeting exanthem, mild fever, pain and swelling of joints and tender enlargement of lymph nodes. The disease runs a benign course of from one to four weeks and ends in complete recovery.

GONCE, Madison, Wis.

Skin Diseases; Allergy

EXPERIMENTAL EVIDENCE THAT LESIONS WITH THE BASIC CHARACTERISTICS OF RHEUMATIC CARDITIS CAN RESULT FROM ANAPHYLACTIC HYPERSENSITIVITY. ARNOLD R. RICH and JOHN E. GREGORY, Bull. Johns Hopkins Hosp. **73**:239 (Oct.) 1943.

In rabbits with experimental serum sickness valvular and myocardial lesions occurred which closely resemble those of rheumatic carditis and provide some support for the view that specific rheumatic lesions may be manifestations of an anaphylactic hypersensitive reac-

tion. The authors do not claim to have reproduced the disease picture as it occurs in man or to have settled the question of the pathogenesis of rheumatic fever.

LITTLE, New York.

CRITICAL EVALUATION OF SKIN TESTS IN ALLERGY DIAGNOSIS. LOUIS TUFT, *J. Allergy* **14**:355 (July) 1943.

A comprehensive review of the status of cutaneous tests is presented. The author recognizes that there has been and still is criticism of cutaneous tests and of the methods of making them. He offers a number of sound and reasonable suggestions to meet these criticisms and to establish a recognized laboratory procedure.

HOYER, Cincinnati.

INHALATION OF OXYGEN AND 1:100 EPINEPHRINE HYDROCHLORIDE PLUS FIVE PER CENT GLYCERIN FOR THE RELIEF OF ASTHMATIC ATTACKS. STEPHEN D. LOCKEY, *J. Allergy* **14**:382 (July) 1943.

The addition of 5 per cent glycerin to a 1:100 solution of epinephrine hydrochloride relieves the dryness and irritation that result from the inhalation of epinephrine hydrochloride solution alone. The formula is given, and the method of preparation is described.

HOYER, Cincinnati.

TREATMENT OF ASTHMA AND HAY FEVER. A CONFERENCE BY STAFF MEMBERS OF CORNELL UNIVERSITY MEDICAL COLLEGE AND OF THE NEW YORK HOSPITAL. HARRY GOLD, ROBERT A. COOKE, C. H. WHEELER and JANET TRAVELL, *New York State J. Med.* **43**:1224 (July 1) 1943.

The term "hay fever" is used to represent all types of nasal allergy. Pathologically there are two types: vasomotor (with acute and completely reversible reactions) and hyperplastic (with chronic and nonreversible changes in tissue). The treatment depends on avoidance of the cause, immunization and symptomatic medication. The patient may move to pollen-free areas, he may live in air-conditioned surroundings, he may eliminate certain household agents, e. g., pillows, mattress, chairs, pets, foods, insecticides. As for treatment of symptoms, little can be done with drugs. In general, local nasal treatments (sprays, cauterization and packs) are to be avoided, for they increase the irritability of the tissues and their action is only temporary. As yet there is insufficient evidence that deficiency of any vitamin or dyscrasia of any endocrine gland has much to do with allergy save as it affects the general health. Foods, contrary to popular belief, "rarely cause trouble," but air-borne substances are common factors. Adenoids, tonsils and teeth must be investigated, but the "type of infection" may be hard to determine. Autogenous vaccines are preferred to "stock" vaccines. Cultures from the submucosa are preferable to cultures from the surface. Cooke makes the following comments: 1. Rarely is surgical treatment indicated for a patient under 25 years of age. 2. Allergy due to inhalants or foods should not be treated with allergens before or after operation. 3. Surgical work must be "superlatively well done." 4. Operations on sinuses must remove infected tissue and secure "drainage"; turbinates must be conserved; resection of the septum is done chiefly to make the surgical approach to a sinus easier. 5. Sinuses are often operated on piecemeal, incompletely or too late. 6. Patients (for surgical treatment) must be selected

with an eye to their physical condition. Not much can be expected when chronic pulmonary fibrosis is present.

Cooke speaks of asthma as (1) atopic, in which the cause is determinable by cutaneous tests, or (2) infective. The more difficult asthmatic patients are children who are continuously asthmatic but not completely disabled. If contact with an allergen is unavoidable, one must try to immunize the patient. This may require weeks, months or years and is vitiated by intercurrent infections of the respiratory tract, which often precede sinusitis and asthma. "Children up to 18 years need little attention to the sinuses if recurring infections can be controlled, and the early removal of tonsils and adenoids is one of the best methods of control." Infections of sinuses, especially those of the antrums, are the most frequent causes of infective asthma. Teeth are, of course, important foci but are less important than other sources.

Summary by Dr. Walter Modell: The treatment of hay fever depends on whether the condition is of the vasomotor or the hyperplastic type. If it is of the former type, avoid the cause, immunize and treat symptoms. If it is of the latter type, permanent changes of the tissues are likely, infection is probably present and recourse must be had to the use of vaccines, surgical procedures or purely symptomatic treatment. Patients with urgent symptoms—bronchial obstruction, for example—may require removal of bronchial plugs by suction or administration of oxygen. Oxygen is given by catheter rather than by mask. Dehydration sometimes helps bronchial obstruction. A diet low in salt and in sodium ash, together with sodium or potassium iodide internally, plus catharsis may afford relief. Severe reactions following the administration of allergens may require solution of epinephrine hydrochloride subcutaneously or, in rare cases, intravenously.

VOORHEES, New York. [ARCH. OTOLARYNG.]

AN EPIDEMIC IN CHILDREN, CHARACTERIZED BY DIVERSITY OF LESIONS IN SKIN AND MUCOUS MEMBRANES, PROBABLY CAUSED BY STREPTOCOCCUS PYOGENES. P. B. MUMFORD and A. G. HEPPLESTON, *Brit. J. Dermat.* **55**:143 (June) 1943.

The authors describe a nonfatal epidemic infection affecting all of 27 children, aged 2½ to 5 years, in a colony of evacuees and several members of the adult staff. It persisted with remissions for more than six months.

About half the children had inflammatory lesions of the nose, eyes, mouth and skin. Six were confined to bed and isolated with pyrexia and eruptions of varying severity. The matron had a sore throat. The nursing sister in charge of the children had a papulovesicular eruption of the extensor aspects of the limbs, without effect on her general health.

The distribution and appearance of the lesions in the children suggested first an external irritant. Exposed areas of skin and mucous membranes were involved; the effects of constant scratching and rubbing were obvious, and constitutional disturbance was considered to be the result of secondary infection. Extensive patch tests with a rare type of grass with which the children's playground had been sown were made on the children with the worst eruptions, but all reactions proved negative. Within a few weeks many more children were affected, and several were toxemic, with high temperature, rigor and prostration. As most of the colony were becoming involved and the epidemic was growing out of control, bacteriologic investigations

were undertaken. A high proportion of patients were found to be harboring hemolytic streptococci of group A type 4. Therapy with sulfonamide compounds was introduced. Rapid amelioration of general and local symptoms followed, but every "cured" patient had a relapse after fresh contact with other children.

BLUEFARB, Chicago. [ARCH. DERMAT. & SYPH.]

A CASE OF PSEUDOMEMBRANOUS INTERTRIGO. ALICE CARLETON, Brit. J. Dermat. **55**:154 (June) 1943.

The author reports a case of rebellious pseudomembranous intertrigo in a girl aged 7 months. There was a strong clinical resemblance to both cutaneous diphtheria and moniliasis. The organisms producing the disease in this instance were staphylococci, streptococci, *Pseudomonas pyocyanea* and *Proteus vulgaris*.

BLUEFARB, Chicago. [ARCH. DERMAT. & SYPH.]

REACTION-PRODUCING ANTIGENS IN ECZEMA OF INFANCY AND CHILDHOOD. P. W. FARMER JR., M. J. Australia **2**:5 (July 3) 1943.

The results of cutaneous tests in 50 cases of eczema in children are reported. Half the patients tested were between 8 months and 5 years of age, and the remainder were up to 13 years; 32 of the patients had bronchial asthma in association with eczema. By far the commonest reaction-producing antigens were horse dander, egg white and grass pollens.

GONCE, Madison, Wis.

Surgery and Orthopedics

POTASSIUM AND THE CAUSE OF DEATH IN TRAUMATIC SHOCK. ALEXANDER W. WINKLER and HEBBEL E. HOFF, Am. J. Physiol. **139**:686 (Sept.) 1943.

Increase in the concentration of potassium in serum has been repeatedly reported in various types of secondary shock. It has been suggested that this elevated concentration of potassium may be an important factor in producing the characteristic picture of traumatic shock and may contribute to the fatal outcome. On the other hand, the picture of potassium poisoning is totally unlike that of traumatic shock. Also, concentrations of potassium considerably higher than those commonly found in the serums of persons with shock are necessary in order to elicit any clinical evidences of intoxication. The present study endeavors to define as exactly as possible the role of potassium in one variety of traumatic shock.

The authors conclude that the concentration of potassium in serum consistently increases when secondary shock is induced by reestablishment of circulation in an ischemic limb. Death usually occurs with respiratory failure prior to or simultaneous with cardiac arrest and is usually not due to potassium poisoning. Concentrations of potassium in the serum while both respiration and heart are active in the shocked animal seldom exceed 8 millimols per liter. These levels are too low to cause any circulatory embarrassment; only minor electrocardiographic changes are induced. Exceptionally, death may be due to cardiac arrest from spontaneous autointoxication with potassium. After respiratory arrest there may be a rapid agonal elevation of the serum potassium. Such increases are the result and not the cause of the terminal event.

NOURSE, Cleveland.

THE TREATMENT OF CONNECTIVE TISSUE FIBROSARCOMA WITH SURGERY AND RADIUM. MILTON FRIEDMAN, Bull. Hosp. Joint Dis. **4**:66 (Oct.) 1943.

The author summarizes his conclusions as follows: "Local resection of a connective-tissue fibrosarcoma is commonly followed by a recurrence. Post-operative x-ray therapy, even in very large doses, will prevent only a small percentage of recurrences. The post-operative insertion of interstitial radium, in the form of radium needles or radon seeds, permits effective cancericidal irradiation of the tumor-bearing area. However, this procedure can be employed only in the case of those tumors which are located at a safe distance from bone or large blood vessels, because the large dose necessary to prevent recurrence may cause serious damage to these structures."

Two cases are reported in which this method was employed. The first patient was a girl 13 years old who had an infiltrating tumor in the lateral aspect of the right hip. Operative removal and treatment with radium took place in March 1940, and there had been no recurrence up to the time of writing. The second patient was a man 52 years old who was similarly treated in 1937; there had been no recurrence.

LESLIE, Evanston, Ill.

THE DESTRUCTIVE ACTION, IN VIVO, OF DILUTE ACIDS AND ACID DRINKS AND BEVERAGES ON THE RATS' MOLAR TEETH. E. J. McCURE, J. Nutrition **26**:251 (Sept.) 1943.

The results of these experiments on the effect of dilute acids on rats' teeth in vivo suggest the possibility that the oral surfaces of the teeth may be affected by acid fluids passing through the oral cavity. Any association of these effects with the initiation of dental caries remains to be determined.

FREDEEN, Kansas City, Mo.

FEET OF NORMAL CHILDREN. MEINHARD ROBINOW, MARGARET JOHNSTON and MARGARET ANDERSON, J. Pediat. **23**:141 (Aug.) 1943.

This is a study of lateral roentgenograms of the weight-bearing foot. The roentgenograms were analyzed according to a method first described by Bertani and Moreau and published in the *Revista Argentina de Reumatologia*, December 1937. Calculation of the frequency distribution showed that in the group studied all the measurements fell within the range of normal variations. There were remarkably small changes in the arch with age, which shows that the arch is well developed relatively early in life. Removing all the load from one foot made the arch of that foot higher, but doubling the load on the foot had no appreciable effect. Shifting the main load to the anterior part of the foot resulted in a distinct flattening of the arch. That seems to show that the stress on the longitudinal arch is proportional to the weight born on the ball of the foot. A significant correlation was found between flatfoot, as shown by the roentgenograms, and pronation of the feet. In the films for older subjects there was a correlation between flattening of the arch and increased weight-length ratio, which tends to confirm the clinical impression of association between obesity and flattened arches. There was no correlation between such flattening and the age at which the children began to walk, nor did rickets appear to be involved in the causation of flatfoot. Genetic analysis suggested the possibility of a hereditary factor in the occurrence of flatfoot.

SONTAG, Yellow Springs, Ohio.

Teeth and Dentistry

IDIOSYNCRASY TO METALLIC MERCURY, WITH SPECIAL REFERENCE TO AMALGAM FILLINGS IN THE TEETH. MURRAY H. BASS, J. Pediat. 23:215 (Aug.) 1943.

Idiosyncrasy to mercury may give rise to many curious clinical pictures. In sensitive persons the application to the skin of ointments containing small amounts of mercury may result in various eruptions (urticaria, erythema, edema and bleb formation), fever, at times hyperpyrexia, prostration and even unconsciousness. In children such symptoms are most commonly seen after the application of ointment of ammoniated mercury. The same child may be sensitive to many compounds of mercury. Two girls are described who at different times showed symptoms due to various preparations, mild mercurous chloride taken internally, a solution of mercury bichloride or an ointment of yellow mercuric oxide or of ammoniated mercury applied externally. Metallic mercury itself may also cause symptoms. In a girl shown previously to be highly sensitive to ammoniated mercury ointment, edema of the lips and face developed a day after a tooth had been filed with an amalgam. The filling was left in place and the redness and swelling disappeared in a few days. These symptoms were due to bits of the amalgam deposited on the cheek by the fingers of the dentist. Another child had the following history. At the age of 4 years she was given a dose of mild mercurous chloride, after which there developed a generalized eruption lasting two days. During an attack of chickenpox, application of a blue medicated soap (mercury bichloride) was followed by urticaria. At the age of 7, application to the eyelids of an ointment containing yellow mercuric oxide caused prolonged edema of the lids and face. At 12 and 13 filling the teeth with amalgam had been followed by circumoral swelling and a blotchy eruption on the lips and cheeks. At the age of 14 she was seen with severe, generalized, giant urticaria which had been present for ten days and had not yielded to any treatment. Three weeks previously she had had two teeth filled with amalgam. Symptoms of urticaria had appeared about ten days after this, and it was suspected that the cutaneous lesions might be an evidence of idiosyncrasy to the mercury in the fillings. One of the fillings was removed. This was immediately followed by an aggravation of the symptoms; the child's feet became so edematous with urticaria that she could not wear shoes and her temperature rose to 102 F. The other filling was immediately removed; twenty-four hours later the symptoms disappeared, and the child remained well thereafter. Passive transfer tests with the child's serum showed a strongly positive reaction to ammoniated mercury.

Both mercury poisoning and symptoms of sensitiveness (idiosyncrasy) have been described following the filling of dental cavities with compounds of mercury. A third case of idiosyncrasy to metallic mercury is that of a small boy who had been playing with the metal, had spilled it and in scooping it up had gotten it against the skin of the abdomen and genitalia, resulting in a severe erythema of those parts, lasting for several days and accompanied by eosinophilia.

In summary, 3 cases of idiosyncrasy to metallic mercury are described; all the patients were children and all showed symptoms referable to the skin. In 2 instances metallic mercury applied to the skin was the active agent. In 2 amalgam fillings were the etiologic factor. In 1 of these symptoms of severe urticaria

continued until removal of the fillings. This cause of urticaria may be more common than is ordinarily supposed.

SONTAG, Yellow Springs, Ohio.

ORTHODONTIA. A. C. MIRANDA, Rev. Soc. pédiat. de la Plata 4:97 (Dec.) 1943.

Sucking is a common cause of deformation of the mouth; if a child is given a metal ring or tube with holes in it, sucking is prevented and yet the child has something to put in his mouth. A child should not sleep with his fist between the face and the pillow, nor should he lean his chin on his hand constantly while reading or studying.

Repeated colds cause changes in the nasal structure, and the dryness of the air caused by modern heating puts an extra burden on the mucous glands. The dentist should investigate possible nasal abnormalities or pathologic conditions before he tries to correct irregularities of the teeth.

HIGGINS, Boston.

ORAL PROPHYLAXIS IN CHILDREN. E. DELLA CROCE, Rev. Soc. pédiat. de la Plata 4:115 (Dec.) 1943.

Oral prophylaxis involves careful observation of the mother during gestation, proper diet for the child during infancy and childhood, correction of nasal abnormalities, avoidance of dental caries, prompt filling of cavities, retention of deciduous teeth until the permanent teeth are ready to erupt and avoidance of bad habits, such as sucking the thumb.

HIGGINS, Boston.

Miscellaneous

STUDIES ON SULFAPYRAZINE. HARRY J. ROBINSON, HENRY SIEGEL and OTTO E. GRAESSLE, J. Pharmacol. & Exper. Therap. 79:354 (Dec.) 1943.

The authors conclude that sulfapyrazine and sulfadiazine produce about the same pathologic changes in rats after prolonged administration, that alkalization of the urine can lessen or prevent renal concretions and that in equal concentrations in the blood the two drugs are equally effective against experimental pneumococcic, streptococcic and staphylococcic infections.

PILCHER, Cleveland.

ANCIENT PROCESSES IN A SCIENTIFIC AGE. C. ANDERSON ALDRICH, New Orleans M. & S. J. 96:2 (July) 1943.

The author stresses the point that infants have natural rhythmic reactions for feeding, intestinal evacuations and sleep. The pediatrician's effort should be to educate the parents in the technic of preserving these normal physiologic tendencies.

In the child's second year effort is to be expended on teaching the parents that a child must be allowed normally to expand his urge to walk, to run, to play, to handle things, to take things apart and to fit them together. Freedom to do this must be accomplished by removal of breakable and valuable objects and by approval rather than restraint of childish efforts, since the latter leads only to negativism.

A tolerant attitude to infantile behavior enables one to understand growth in later years, for example, to realize that a child reads when his brain has developed to the reading stage, not when he achieves a certain chronologic age. One can understand that handedness should be respected and that masturbation by an infant is only a stepping stone in sexual growth. One can

also understand the problems of adolescents and realize that it is right for them to mature, to take on responsibilities, to make love, to mate and to have children of their own. When adults have accomplished that degree of understanding, they, too, have really grown up.

BERKLEY, Beverly Hills, Calif.

ADDITIONAL MANIFESTATION OF SULPHATHIAZOLE TOXICITY. E. PRESS and M. KENNERSTEIN, Arch. Dis. Childhood **18**:50 (March) 1943.

Two cases are presented in which during treatment with sulfathiazole renal irritation, oliguria and azcemia developed, causing death. These disturbances were not accompanied by formation of calculi or anatomic changes sufficient to account for them. It is suggested that they are a toxic manifestation of sulfathiazole, which causes a change in function rather than in structure of the nephron.

KELLY, Milwaukee.

A CASE OF PHENOTHIAZINE POISONING IN SYDNEY. L. I. H. GRANT, M. J. Australia **2**:27 (July 10) 1943.

A girl aged 7½ years was given 2 Gm. of phenothiazine (thiodiphenylamine) a day for seven days, in the treatment of threadworms. On the ninth day the child's blood showed 1,810,000 red cells per cubic millimeter with some nucleated cells present, and a hemoglobin value of 40 per cent. A transfusion of fresh citrated blood and administration of a preparation of iron brought about complete restoration of the normal blood picture. The author cites a number of other reports of acute hemolytic anemia secondary to treatment with phenothiazine, and he states that "although this form of treatment is effective in intractable cases of threadworm infestation and attractive to administer, surely we cannot countenance its continued use."

GONCE, Madison, Wis.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

HEYWORTH N. SANFORD, M.D., *President,*
in the Chair

April 18, 1944

Myocarditis in Childhood. (Inaugural Thesis).
DR. SIMON A. WILE.

So-Called Idiopathic Cardiac Hypertrophy in Infants. DR. BENJAMIN M. GASUL.

Rheumatic Fever in the Army from the Pediatrician's Point of View. MAJOR MARTIN WENDKOS, Medical Corps, Army of the United States.

The material presented embodied the results of experiences with rheumatic fever as it occurred in epidemic proportions among soldiers in and around Chicago during the years 1943 and 1944. Particular emphasis was placed on the diagnostic features of the disease and the reliability of symptoms: Physical signs and electrocardiographic findings were individually evaluated. In the main, it was noted that information obtained from frequent sequential electrocardiograms was the most dependable and incontrovertible, the repeated electrocardiograms being found essential because of the transient nature of the aberrations in these records. The nonspecific nature of the changes was also stressed, and it was demonstrated that other acute infections in which the heart is similarly involved can produce disturbances in conduction comparable to those which occur in rheumatic fever. The electrocardiographic aberrations on which the greatest reliance was placed consisted of first, second and third degree auriculo-ventricular heart block, delayed intra-auricular and intraventricular conduction, sinus bradycardia, wandering pacemaker and changes in the polarity, amplitude or configuration of the T wave in either the limb or the chest leads.

On the basis of the response to the hypodermic administration of $\frac{1}{25}$ grain (2.4 mg.) of atropine sulfate, hypervagotonia was shown to be operative in the production of the various disturbances in conduction, a finding which extends the original work of Bruenn. It was demonstrated that first degree auriculoventricular heart block, second degree auriculoventricular heart block, nodal rhythm, delayed intra-auricular conduction and wandering pacemaker, which were accompaniments of active carditis in the disease, could be temporarily abolished by the parasympatholytic action of the drug. Evidence based on an original testing method developed by the author was presented to indicate that, conversely, the supplementary use of a sympatholytic drug such as ergotamine tartrate might provoke significant abnormalities of conduction which had not been registered in an initial record during the active phases of the rheumatic state. This procedure was therefore recommended as a helpful diagnostic adjunct for use when the identification of the rheumatic infection requires confirmatory objective data. A further analysis of the clinical material also revealed that the differential diagnosis between acute rheumatoid arthritis and

acute rheumatic fever may be difficult because cardiac involvement is a feature common to both syndromes and because the arthritic manifestations are not infrequently indistinguishable. It was suggested also that the two diseases may have fundamentally similar causes, the evolution of the arthropathy differing because of immunologic factors which are not too well understood.

The sedimentation rate of the erythrocytes was generally found to be a reliable index of active rheumatic infection, but in an occasional case, in spite of a normal sedimentation time, the serial electrocardiograms continued to show significant alterations indicative of active myocardial changes.

Tonsillectomy in childhood was observed not to be a deterrent to the subsequent development of a primary attack of rheumatic fever or of rheumatic recurrences. In the section of population on which this report was based the frequency of rheumatic fever as compared with that of scarlet fever was striking, even allowing for the relatively high degree of immunity young adults possess against scarlatina. The incidence of rheumatic fever seemed to be higher in persons from families in which rheumatic infection had previously occurred, a fact which supports the belief in a hereditary predisposition to the disease. Because of this fact and because a close parallelism was found in this survey between the rising incidence of hemolytic streptococcal infections of the respiratory tract and the incidence of rheumatic fever, it was suggested that care should always be taken to exclude the possibility of a rheumatic infection in any child who comes from a rheumatic family and who is suffering from a hemolytic streptococcal infection of the respiratory tract or from scarlet fever during the winter or spring months, especially in states where the disease is endemic. It was emphasized that detection may not always be easy because arthritic manifestations are frequently insignificant in children suffering from rheumatic fever and because of the more benign forms the cardiac involvement is likely not to be severe enough to produce clinically recognizable cardiac enlargement, endocardial murmurs or a pericardial friction rub. It was therefore the recommendation of the author, in order to establish more valid concepts concerning the true incidence, the seriousness and the prognosis of rheumatic fever in its varying increments of severity, that electrocardiograms, obtained either serially or after the administration of ergotamine tartrate, be employed routinely in all cases of hemolytic streptococcal infections of the upper part of the respiratory tract, especially during the winter and spring months.

DISCUSSION

LT. COL. IRVING WRIGHT (Medical Consultant, Sixth Service Command): This paper is interesting. Perhaps the most significant new note which is recognized is the reaction produced in the case of questionable carditis by the use of ergotamine. It may turn the doubtful diagnosis into a more decisive one and therefore be of considerable use in the treatment of rheumatic fever. Probably it will help also in following the course of the disease if one can determine when the reaction is no longer existent. Not infrequently

we encounter in the army persons with a syndrome as to which it is difficult to differentiate between rheumatoid arthritis and rheumatic fever. I should like to call attention to 200 cases of rheumatoid arthritis in which after periods of months or years the PR interval became prolonged and in 24 per cent of which there developed iritis or pneumonia of a so-called rheumatic fever type and other changes considered to be part of the syndrome characteristic of rheumatic fever.

Major Wendkos did not have time to discuss some recent observations in reference to treatment of this syndrome, and I thought some observations made in the army might be of interest. Penicillin would naturally come to mind for serious trial, since it is specific for so many diseases in the streptococcic group. I have had reports from the National Research Council, the Army Service Forces and the Army Air Force on the use of penicillin in rheumatic fever. Unfortunately, the results have been so universally unsatisfactory that orders have been issued which will effect a discontinuance of its use for this disease in the army hospitals.

Salicylates have been given empirically for a long time, but more accurate data about their effects are becoming available. In the first place, Brody and others have been able to perfect a method by which the level of salicylic acid in the plasma can be measured. Thus the first step in removing salicylate therapy from the empiric field has been taken. There is an error of less than 7 per cent in Brody's method. In symptomatic treatment 3 to 6 Gm. of sodium salicylate a day gave a blood level of 250 micrograms per cubic centimeter. Massive doses, 10 to 20 Gm. a day, resulted in a blood level of 350 micrograms per cubic centimeter. This result is being checked in a good many hospitals at present, but reports of Colburn's work might be mentioned. In 19 of 43 patients treated with 2 to 6 Gm. a day polycyclic rheumatic fever developed; 16 of these had mitral stenosis. In other words, all but 3 of these had mitral disease as a residual. Eighteen patients, one half of whom gave evidence of the presence of myocarditis on admission, were treated with 10 Gm. or more daily, and heart disease developed in none of them. In addition to that rather significant finding, the general inflammatory reaction subsided more rapidly than with the former dosage. These figures are striking, though the series is rather small. In general, Colburn's work has stood the test of time in other fields, and the army is giving his findings serious consideration. In six months or a year we shall have a larger series and shall know whether or not the preliminary results were reliable.

One other finding of significance comes from the work of Link and his associates at the University of Wisconsin. They were able to produce hypoprothrombinemia in rabbits by salicylate therapy. Vitamin K protected the animals against this effect. The work has been checked in human beings by Meyer, of Wisconsin, and Shapiro, of New York, and it is true that even moderate doses produce moderate hypoprothrombinemia in human beings. No effect is noted on clotting in vitro. As early as fifty years ago Binz found that the administration of salicylates produced tendencies toward bleeding. Certainly this fact has no great statistical significance, because there have been many thousands of cases of rheumatic fever in the army and the amount of salicylates given has been large, yet

hemorrhage has been rare. Whether it is because the diet is adequate I do not know, but that seems likely. There will be isolated cases in which hemorrhagic manifestations occur. Vitamin K may be administered in these cases.

DR. STANLEY GIBSON: Major Wendkos' paper is most interesting. I was particularly struck with the frequency of electrocardiographic changes in the absence of clinical evidence of cardiac disease. It seems to me that the rheumatic picture as it is encountered among young men in the army is a somewhat different disease from that which is seen in children in civil life. Certainly I do see a high percentage of patients with definite and early physical signs of cardiac involvement. Often there is appreciable enlargement of the heart, together with significant murmurs which have not been present previously. Moreover, I have taken a good many electrocardiograms in my cases without finding nearly so high a percentage of abnormal electrocardiograms as Major Wendkos. Perhaps I have not taken them often enough or have been too liberal in my interpretation of the normal electrocardiogram. Doubtless I am missing a number of cases in which cardiac involvement is present; yet I have followed over a long period of years a number of children who had typical rheumatic arthritis but in whom no signs of cardiac disease have appeared during the years. It would seem to me that definite cardiac injury if permanent should have manifested itself at least in those who have been followed for ten or fifteen years.

MAJOR MARTIN WENDKOS: With reference to Dr. Gibson's discussion, we examined our patients daily, sometimes twice a day, for from thirty to sixty days; therefore, any opinion as to the presence or absence of a lesion was based on observations during that period. The reason I raised the question about possibly missing the diagnosis of rheumatic fever in the absence of a manifest endocardial lesion was that in surveys of school children cases were encountered in which no antecedent diagnosis of rheumatic fever had been made. From what we know of mitral stenosis, we feel that rheumatic fever is the cause in 99 per cent of the cases; therefore, it is my supposition that these children had rheumatic fever that escaped detection, and it is because of interest in the epidemiology and control of the disease that I stress these diagnostic factors, so that the true incidence may be more properly appraised.

I do not recommend that atropine be used routinely. I merely injected the drug to show that the electrocardiographic changes are the result of hypervagotonia. There were no ill effects from the drug, and it did not affect the course of the disease.

LT. COL. IRVING WRIGHT: I believe Colburn's work was all from the same series and was carefully controlled; it was done in the navy. I know Colburn well enough to know that he would do a well controlled study; it has appeared in several publications.

I should like to add that a great many cases of rheumatic fever are being missed. A review was made by cardiologists in each of five cities of 1,000 cases of persons who had been rejected for army service, and that group of experts decided that in 26 per cent of the cases rheumatic heart disease had not been diagnosed and there was no definite history of previous rheumatic fever.

Book Reviews

Air-Borne Infection; Some Observations on Its Decline. By Dwight O'Hara, M.D. Price, \$1.50. Pp. 114, with 11 charts. New York: The Commonwealth Fund, 1943.

This small volume is an outstanding contribution to medical literature. It presents a thoughtful analysis and philosophic consideration of the history of air-borne infections in the commonwealth and state of Massachusetts. There are chapters on smallpox, diphtheria, the common cold, pneumonia, streptococcic infections, rheumatic fever and tuberculosis. The trends in mortality are studied in relation to all factors which may be considered to operate in the fields of preventive medicine, treatment of disease and public health. These include sanitation, standards of living, nutrition, isolation of foci of infection as in tuberculosis, treatment and specific immunizing measures. It is shown that in addition to all conscious efforts to control the diseases under discussion, there are probably other ameliorative factors, little understood at present, which are partly responsible for the decreases in mortality. This seems to be particularly true of measles and scarlet fever. The author is an enthusiastic supporter of measures for active immunization, except that in the case of scarlet fever he feels too much emphasis is put on only one aspect of the disease, the rash. He doubts the advisability of passive immunization except under exceptional circumstances or in a case of tetanus in which the patient has not been actively immunized. At the present time the best immunity to measles, mumps and chickenpox is obtained by having the disease in childhood. This immunity as well as immunity to other air-borne infections is probably kept up throughout life by the repetition of subclinical attacks. The last two chapters deal with the relationship of biologic inheritance, environment and the aging process to health and resistance to disease. The author reveals deep wisdom in his understanding and correlation of facts. The reviewer feels that this book could be read with interest by every member of the medical profession.

The Epidemiology of Rheumatic Fever and Some of Its Public Health Aspects. Written by John R. Paul, M.D., and other contributors for the American Heart Association. Second edition. Price, none given. Pp. 163, with 31 illustrations. New York: Metropolitan Life Insurance Company, 1943.

The author regards rheumatic fever as a specific disease, though he admits there are certain arguments against this assumption. One argument hinges on the relationship of rheumatic fever to streptococcic infections. Until the question of whether hemolytic streptococci are the only infectious agents in rheumatic fever has been answered, the concept of this condition as a clinical entity should not be discarded.

Midchildhood is the period of greatest susceptibility to first attacks, partly, in all probability, because of more frequent exposure to infection during this period.

The prevalence of rheumatic fever is determined by both environment and inherited tendencies. Among the environmental factors, climate, season and living conditions are important. Among the elements in living conditions which seem to be important are poverty,

crowding and dampness. There is also good evidence from a study of rheumatic families that there is an inherited tendency toward the acquisition of rheumatic fever.

The author emphasizes the fact that public health programs have lagged behind other aspects of the study of this disease. Although many agencies have been interested, their efforts have not been coordinated. First of all, physicians, nurses and social workers must be educated to the importance of the problem. Efforts should then be centered on early recognition of the disease and adequate care for those who have already contracted it.

This excellent study deserves a wide reading among students of rheumatic fever.

Micrurgical and Germ-Free Techniques; Their Application to Experimental Biology and Medicine; a Symposium. Ed. 1. Edited by James A. Reyniers. Price, \$5.00. Pp. xiv and 274, with 94 illustrations and 17 tables. Springfield, Ill.: Charles C Thomas, 1943.

Micrurgy is a basic technic adapted to the manipulation and observation of microscopic objects, animate or inanimate. With this definition, the first chapter of the symposium edited by James A. Reyniers begins a description of this technic as it is applied, first, to surface chemistry and the study of living cells, second, to botany, and then, with the development of the "germ-free system," to the study of living animals, including the mammalian fetus.

Much of the technical and even of the theoretic aspects of the problem is beyond the scope of interest of the average medical reader. However, the description of the "germ-free" system as developed at Notre Dame, by which animals may be reared for as long as six months under these conditions, is most interesting. Such methods have been carefully and ingeniously planned and offer opportunities for the study of many problems.

Of special interest to pediatricians is the application of the principles of the germ-free system to the control of cross infections in hospitals and institutions in which infants and children are cared for. The effective principles are (1) air conditioning, (2) light barriers and (3) mechanical barriers. At the Cradle in Evanston, Ill., units have been constructed and tested on the basis of these principles.

The Boy Sex Offender and His Later Career. By Dr. Lewis J. Doshay. Price, \$3.50. Pp. 206, with 40 tables and 12 diagrams. New York: Grune & Stratton, Inc., 1943.

"This study was undertaken to investigate the significance of early sex offenses among males for later life behavior, and in particular to determine to what extent these juveniles become a menace to society through the commission of sexual or other offenses in adult years. The study also set itself to discover determining factors in the background, personality and behavior of juvenile sex delinquents that relate to success or failure in adult life, as criteria in the prediction and treatment of similar cases."

The book presents conclusions drawn from a study of the cases which appeared in the clinics of the Children's Court of New York over a period of six years. There is a careful analysis of the factors in the home and community and in the personalities of the parents which might influence each case and a fairly complete study of the personality of each offender.

Perhaps the most significant conclusion is that boys who are guilty of sexual offenses but who do not violate the law in other ways do not commit sexual crimes when they grow up; those who commit both sexual and other offenses present personality patterns which do often bring them in conflict with the law during adulthood but not often for sexual offenses.

This book records the first detailed analysis of this problem. It is well written and interesting throughout.

Manual of Medical Services for Children in Planning For, During and After Evacuation. Prepared by the State Defense Council of Connecticut, with the cooperation of the State Department of Health. Price, 25 cents. Pp. 56. Hartford, Conn.: State Defense Council, 1942.

This manual gives instructions for the preparation, handling and placement of children should evacuation from industrial centers become necessary. Among the "musts" in preparation is the immunization of children to smallpox, diphtheria and tetanus. Children who have contagious diseases should be sent to locations handling such patients rather than evacuated with the well children. Special instructions are given for the care of newborn and premature infants. It is urged that children with psychiatric difficulties be handled separately to prevent the spread of neuroses. Food and medical supplies necessary for the care of children during evacuation are listed.

The material is well organized, and the committees in charge deserve credit for their careful thought and attention to detail.

The Compleat Pediatrician. By W. C. Davison. Fourth edition. Price, \$3.75. Pp. 256. Durham, N. C.: Duke University Press, 1943.

The fourth edition of this well known textbook has been entirely revised and brought up to date as to treatment, and there are several additions. There is

no increase in the total pages, however, for in this edition a bibliography has not been appended. This book becomes better and better; no physician who works with children should be without it.

State Programs for Care of Children with Rheumatic Fever Under the Social Security Act, Title V, Part 2. United States Department of Labor, Children's Bureau. Pp. 5, with no illustrations. Washington, D. C.: Superintendent of Documents, Government Printing Office, 1943.

In 1939 additional funds for the care of crippled children were authorized by Congress with the understanding that a portion of these funds be used for the care of children with rheumatic fever.

The typical program administered by a state agency for the care of crippled children serves at present only a small area, one to four counties. Children with heart disease or conditions leading to heart disease are referred to this agency by physicians, schools, hospitals and other institutions. A pediatrician acceptable to the American Board of Pediatrics is employed by the state, and consulting services are provided for social service. Nursing and educational needs are also met.

The Microscope and Its Use. By Francisco J. Muñoz in collaboration with Dr. Harry A. Charipper. Price, \$2.50. Pp. 320, with 122 illustrations. Brooklyn, N. Y.: Chemical Publishing Co., Inc., 1943.

This is a technical book on the microscope in non-technical language, written by a technical microscopic consultant and a professor of biology. There are chapters on the historical development, types, structure and use of simple and compound (both monocular and binocular), stereoscopic, metallurgic and polarizing microscopes and their accessories. The authors describe the various types of illumination and the adjustment of illuminating equipment and explain the common errors in the use of the microscope. There is a chapter on the use of the microtome, and a glossary and a bibliography are included. The book is well illustrated and written in essentially nontechnical language. It fills a need for an introduction to the use of the microscope for any one who must use this instrument without thorough instruction in all the finer details of its adjustment.

News and Comment

PERSONAL NEWS

Sabbatical Leave for Dr. Henry J. Gerstenberger.—Dr. Henry J. Gerstenberger is taking a year's sabbatical leave beginning Aug. 28, 1944, the date on which the school year of the Western Reserve University School of Medicine began. Dr. John A. Toomey has been appointed acting head of the department of pediatrics at the School of Medicine and acting director of pediatrics at the University Hospitals and at the City Hospital, Cleveland, institutions affiliated with the School of Medicine.

Dr. Gerstenberger will use his leave in writing a history of the Babies and Childrens Hospital of Cleveland and also a history of the development of preventive medicine and social medicine (the infant and child wel-

fare and the antituberculosis movement) in Greater Cleveland.

GENERAL NEWS

American Board of Pediatrics.—Examinations by the American Board of Pediatrics, Inc., will be held on the following dates: March 2, 1945, a written examination, locally, under a monitor, for all physicians planning to take the oral examination in the spring; April 14 or 15, 1945, an oral examination in New York; May 19 or 20, 1945, an oral examination in Chicago.

The deadline for applications for the first two examinations is Dec. 15, 1944; for the oral examination in Chicago, Jan. 19, 1945.

No more applications for fall examinations can be accepted.

Directory of Pediatric Societies *

INTERNATIONAL

INTERNATIONAL ASSOCIATION OF PREVENTIVE PEDIATRICS

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

INTERNATIONAL CONGRESS OF PEDIATRICS

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Charles F. McKhann, University Hospital, Ann Arbor, Mich.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston. Time: Postponed indefinitely.

INTERNATIONAL CONGRESS FOR THE PROTECTION OF INFANCY

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

ARGENTINE PEDIATRIC SOCIETY OF BUENOS AIRES

President: Dr. Martín Ramón Arana, 1809 Rodríguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo La-guia, Cerrito 1179, Buenos Aires.

ASSOCIAÇÃO PAULISTA DE MEDICINA, SECTION ON PEDIATRICS

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Paulo de Barros Franca, Av. Brigadeiro Luiz Antonio 393, 1º Andar, São Paulo, Brazil.

BRITISH PAEDIATRIC ASSOCIATION

President: Prof. L. G. Parsons, 58 Calthorpe Rd., Five Ways, Birmingham.
Secretary: Dr. Donald Paterson, 27 Devonshire Pl., London, W. 1.

DANISH PEDIATRIC SOCIETY

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

NEDERLANDISCHE VEREENIGING VOOR KINDER-GENEESKUNDE

President: Dr. J. H. G. Carstens, Servaasbolwerk 14a, Utrecht.
Secretary: Dr. R. P. van de Kastele, Laan van Poot 340, 's Gravenhage.
Place: Different places. Time: Three times a year.

PAEDIATRICKÝ SPOLOK NA SLOVENSKU

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialkstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Angel A. Aballí Arellano, 17 No. 609 Vedado, Habana.
Secretary: Dr. Julio G. Cabrera Calderin, Hospital Mercedes L y 21 (Vedado), Box 2430, Habana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Fernando López Clares, 12/a. Medellín 191, Mexico.
Secretary: Dr. Jesus Gómez Pagola, Versalles 64, Mexico.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. E. Santos Mendoza.
Secretary: Dr. P. Oropeza, Hospital de Niños, Caracas.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Jose Alberto Praderi, Eduardo Acevedo 1132, Montevideo.
Secretary: Dr. Alfredo Ramon Guerra, Paysandú 824, Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Franklin P. Gengenbach, 1850 Gilpin St., Denver, Colo.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S
HOSPITAL SECTION

Chairman: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly, Mass.

AMERICAN PEDIATRIC SOCIETY

President: Dr. James L. Gamble, 300 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES
OF CHILDREN

President: Dr. R. R. Struthers, 906 Drummond Medical Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Joseph A. Johnston, Henry Ford Hospital, Detroit.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Eugene Smith, 385-24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Warren R. Sisson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. C. G. Ashley, 833 S. W. 11th Ave., Portland, Ore.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. Arild E. Hansen, University of Minnesota, Minneapolis.
Secretary-Treasurer: Dr. Albert V. Stoesser, 205 W. University Hospital, Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester.
Time: January, April, July and October.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver.

SOUTHERN MEDICAL ASSOCIATION, SECTION
OF PEDIATRICS

Chairman: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.
Secretary: Dr. Angus McBryde, 604 W. Chapel Hill St., Durham, N. C.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Amas Gipson, 948 Forrest Ave., Gadsden.
Secretary-Treasurer: Dr. Ruth Berrey, 2021-6th Ave. N., Birmingham.

ARIZONA PEDIATRIC SOCIETY

President: Dr. Vivian Tappan, San Clemente, Tucson.
Secretary: Dr. Hilda Kroeger, Arizona State Health Dept. (Maternal and Child Welfare Division), Phoenix.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION
ON PEDIATRICS

Chairman: Dr. William C. Deamer, University of California Hospital, San Francisco.
Secretary: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Ludo Von Meysenbug, Box 3356, Daytona Beach.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. T. F. Davenport, 104 Ponce de Leon Ave. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB
OF CONNECTICUT

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Time: Three meetings a year.

ILLINOIS STATE MEDICAL SOCIETY, SECTION
ON PEDIATRICS

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Mark L. Floyd, Children's Hospital, Iowa City.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION
ON PEDIATRICS

Chairman: Dr. A. Clement Silverman, 608 E. Genesee St., Syracuse.
Secretary: Dr. Albert G. Davis, 307 Gas and Electric Bldg., Utica.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA,
PEDIATRIC SECTION

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

MICHIGAN STATE MEDICAL SOCIETY,
PEDIATRIC SECTION

Chairman: Dr. Charles F. McKhann, University Hospital, Ann Arbor.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. E. W. Hancock, 820 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. John M. Thomas, 1102 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Arthur H. London, 1105 W. Main St., Durham.
Secretary: Dr. Jay M. Arena, 604 W. Chapel Hill St., Durham.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Ben H. Nicholson, 301 N. W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Lonita Boggs, 301 E. Coffee St., Greenville.
Secretary-Treasurer: Dr. Hilla Sheriff, Wade Hampton Office Bldg., Columbia.

TEXAS PEDIATRIC SOCIETY

President: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Edwin A. Harper, 301 Rivermont Ave., Lynchburg.
Secretary: Dr. Emily Gardner, 1130 W. Franklin St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY,
SECTION ON PEDIATRICS

President: Dr. Andrew Amick, 1021 Quarrier S Charleston.
Secretary: Dr. A. A. Shawkey, Professional Bldg Charleston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND
PEDIATRIC SECTION

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave Cleveland.
Secretary: Dr. L. B. Silber, 10465 Carnegie Ave Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO,
SECTION OF PEDIATRICS

President: Dr. I. Nelles Silverthorne, 170 St. George St., Toronto, Canada.
Secretary: Dr. G. P. Hamblin, 2333 Bloor St. W Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry J. Cohen, 1975 Walton Ave New York.
Secretary: Dr. Walter Levy, 12 E. 88th St., New York
Place: Concourse Plaza Hotel, 161st St., and Grand Concourse. Time: Second Wednesday of each month except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Harry A. Naumer, 37-8th Ave, Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St. Brooklyn.
Place: Granada Hotel. Time: Fourth Wednesday of October, November, February, March and April.

BUFFALO PEDIATRIC SOCIETY

President: Dr. A. Wilmot Jacobsen, 187 Bryant St., Buffalo N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Edward J. Wynkoop, 501 James St., Syracuse.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Morley D. McNeal, 2 N. Sheridan Rd., Highland Park, Ill.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

CINCINNATI PEDIATRIC SOCIETY

Secretary: Dr. T. Sellkirk, 3530 Reading Rd., Cincinnati.
 Place: Children's Hospital, Elland Ave., Cincinnati.
 Time: On call.
 President: Dr. Lloyd K. Felter, 3144 Jefferson Ave., Cincinnati.

DALLAS PEDIATRIC SOCIETY

President: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas, Texas.
 Secretary-Treasurer: Dr. Gladys J. Fashena, 4585 Bel-
 fort, Dallas, Texas.
 Place: Bradford Baby Hospital. Time: 1 p. m., second
 and fourth Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. John J. Pollack, 650 Maccabees Bldg.,
 Detroit, Mich.
 Secretary: Dr. Philip J. Howard, 2799 W. Grand Blvd.,
 Detroit, Mich.
 Place: Wayne County Medical Society. Time: 8:30
 p. m., first Wednesday of each month from October
 to June, inclusive.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRICS
 SECTION (ATLANTA, GA.)

Chairman: Dr. Don F. Cathcart, 478 Peachtree St.
 N. E., Atlanta.
 Secretary: Dr. Harry Lange, 478 Peachtree St., N. E.,
 Atlanta.
 Place: Academy of Medicine, 38 Prescott St. N. E.
 Time: Second Thursday of each month from October
 to April, 8 p. m.

HOUSTON PEDIATRIC SOCIETY

President: Dr. Raymond Cohen, 2300 Caroline St.,
 Houston, Texas.
 Secretary: Dr. Betty Moody, 526 Richmond Rd.,
 Houston, Texas.
 Place: College Inn, Houston. Time: Fourth Monday
 of each month.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Edwin H. Schorer, 1103 Grand Ave.,
 Kansas City.
 Secretary: Dr. H. E. Petersen, Kirkpatrick Bldg., St.
 Joseph, Mo.
 Place: Kansas City General Hospital. Time: On call.

LOS ANGELES COUNTY MEDICAL ASSOCIATION,
 PEDIATRIC SECTION

President: Dr. Oscar Reiss, 2200 W. 3d St., Los
 Angeles.
 Secretary-Treasurer: Dr. Elena Boder, 1830½ Lucille
 Ave., Los Angeles.
 Place: Los Angeles County Medical Headquarters, 1925
 Wilshire Blvd. Time: Second Monday of February,
 April, June, October and December.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND
 THE ACADEMY OF MEDICINE OF BROOKLYN,
 PEDIATRIC SECTION

President: Dr. Abraham M. Litvak, 1145 Eastern Park-
 way, Brooklyn.
 Secretary: Dr. Harold Levy, 750 St. Marks Ave.,
 Brooklyn.
 Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m.,
 fourth Monday of each month, October to April,
 inclusive.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC.,
 SECTION ON PEDIATRICS

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens
 Village, N. Y.
 Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th
 Ave., Flushing, N. Y.
 Place: Queens County Medical Bldg., Forest Hills,
 N. Y. Time: Third Monday of October, January,
 March and May.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA,
 SECTION ON PEDIATRICS

President: Dr. Harry A. Spigel, 2647 Connecticut Ave.,
 Washington, D. C.
 Secretary-Treasurer: Dr. Perry W. Gard, 2520 Wood-
 ley Rd., Washington, D. C.
 Place: Medical Society Bldg., 1718 M St. N. W. Time:
 8 p. m., fourth Thursday of every month.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. F. T. Mitchell, 376 S. Bellevue Ave.,
 Memphis, Tenn.
 Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madi-
 son Ave., Memphis, Tenn.
 Place: John Gaston Hospital. Time: Quarterly.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. John H. Reynolds, 1628 W. Wisconsin
 Ave., Milwaukee.
 Secretary-Treasurer: Dr. F. J. Mellencamp, 324 E.
 Wisconsin Ave., Milwaukee.
 Place: Milwaukee Athletic Club. Time: Second Wednes-
 day of each alternate month, beginning with February.

NEW YORK ACADEMY OF MEDICINE, SECTION
 OF PEDIATRICS

Chairman: Dr. Howard Craig, 175 E. 79th St., New
 York.
 Secretary: Dr. Alfred E. Fischer, 73 E. 90th St., New
 York.
 Place: New York Academy of Medicine, 2 E. 103d St.
 Time: Second Thursday of each month from October
 to May, inclusive, 8:30 p. m.

NORTHERN CALIFORNIA AFFILIATES

President: Dr. Crawford Bost, 400 Post St., San
 Francisco.
 Secretary: Dr. William A. Reilly, 384 Post St., San
 Francisco.
 Time: Second Thursday of September, November,
 January, March and May.

OKLAHOMA CITY PEDIATRIC SOCIETY

President: Dr. William M. Taylor, 1200 N. Walker
 St., Oklahoma City.
 Secretary: Dr. G. R. Felts, 625 N. W. 10th St., Okla-
 homa City.
 Place: Oklahoma Club. Time: Third Thursday of
 each month.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Carl Fischer, Greene and Coulter Sts.,
 Germantown, Philadelphia.
 Secretary: Dr. Sherman Little, 1740 Bainbridge St.,
 Philadelphia.
 Place: College of Physicians, 19 S. 22d St. Time:
 Second Tuesday in January, March, May and
 November.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown, Pa.

Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh.

Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Stanley Meade, 913 Floyd Ave., Richmond, Va.

Secretary-Treasurer: Dr. Louise Galvin, 214 S. Boulevard, Richmond, Va.

Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Herbert Soule, 122 Rutgers St., Rochester, N. Y.

Secretary-Treasurer: Dr. Jerome Glaser, 300 S. Goodman St., Rochester, N. Y.

Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Jerome Diamond, 508 N. Grand Ave., St. Louis.

Secretary-Treasurer: Dr. Mary A. McLoon, 408 Humboldt Bldg., St. Louis.

Place: St. Louis Medical Society Bldg. Time: First Friday of each month from November to June.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Frederick B. Joy, Stimson Bldg., Seattle.
Secretary: Dr. Sherod M. Billington, Medical Den Bldg., Seattle.

Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.

Secretary: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.

Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Campbell Harvey, 35 W. Huron St., Pontiac, Mich.

Secretary: Dr. Harry A. Towsley, University of Michigan, Department of Pediatrics and Communicable Diseases, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (NEW YORK)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.

Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.

Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.

A COMPLETELY SUPPLEMENTED EVAPORATED MILK AND ITS USE AS A FOOD FOR INFANTS

E. W. McCOLLUM, PH.D., AND WILSON GRUBB, M.D.

BALTIMORE

COMPOSITION

About two years ago Dr. Edwards A. Park suggested that a formula be prepared which could be successfully preserved by canning and would constitute a complete food for an infant. He stated that he had previously held the view that the addition of vitamins or vitamin preparations to the diet of an infant was preferable to the inclusion of any extra substances in the infant's basic food. He believed that the public in general could be educated to the use of supplementary vitamins in the feeding of infants.

He had abandoned this view in recent years because of the facts brought out by autopsies on infants dying in the Harriet Lane Home. These studies revealed a surprisingly high incidence of both scurvy and rickets in spite of the educational programs conducted at the children's dispensaries and well baby clinics of Baltimore on the importance of providing supplementary vitamins. He stated that he believed that efforts to educate the public to the use of the necessary supplementary vitamins had progressed as far as possible and that if the infants who still suffered from deficiencies were to be protected a basic food with the necessary vitamins added must be made available. It was on this basis that he was willing to revise his previous concept.

An impetus toward the solution of this problem was recently afforded by the need for an easily transported and easily used complete food for use in feeding large numbers of undernourished children in the rehabilitation of occupied countries. It was felt that on the basis of this

The cost of the infant-feeding study was in great measure defrayed by a grant from the John and Mary Markle Foundation.

The manufacture and assays of the food used in this study were carried out by the staff of the National Dairy Products Corp., Research Laboratories, Baltimore.

From the Department of Biochemistry of the School of Hygiene and Public Health, Johns Hopkins University, and the Harriet Lane Home of the Johns Hopkins Hospital and the Department of Pediatrics, Johns Hopkins University School of Medicine.

need a study of such a complete formula should be carried out with dispatch.

In compliance with this suggestion there was formulated a list of supplements to be added to evaporated milk to produce a complete food for infants.

The following considerations have been kept in mind during the process of perfecting the diet:

Sterility.—The product has been treated with sufficient heat to make it sterile; thus all possible chance of infection is eliminated.

Convenience.—The product is a liquid, the form which is of greatest convenience in preparing a formula, and it is concentrated to permit the physician to alter the feeding by adjustments in the degree of dilution.

Composition.—The product is a completely fortified evaporated milk. Details of the average composition in the form probably most suited to the needs of the medical profession are given in table 1. The contents of each can provide approximately 570 calories. Additional calories may be obtained through the use of added carbohydrates.

The average composition of the test food is shown by the following data:

	Per Cent
Moisture.....	74.0
Total milk solids.....	25.9
Protein (milk).....	7.0
Fat (butterfat).....	7.9
Carbohydrate (lactose)...	9.0
Crude fiber.....	0.0
Calcium.....	0.2
Phosphorus.....	0.2
Iron.....	0.0024

Laboratory analysis showed the following minimum values per 13 fluidounce (14½ avoirdupois ounce) can (400 cc.; 410 Gm.).

Vitamin A.....	2,000 U. S. P. units
Vitamin B ₁	1.0 mg. (333 U. S. P. units)
Vitamin C.....	50.0 mg. (1,000 U. S. P. units)
Vitamin D.....	500 U. S. P. units
Riboflavin.....	3.0 mg.
Nicotinic acid.....	5.0 mg.
Biotin.....	0.015 mg.
Pantothenic acid.....	3.0 mg.
Copper.....	2.0 mg.
Manganese.....	2.0 mg.

Each can of the product was also fortified with 0.4 Gm. of solvent extracted wheat germ oil.

TABLE 1.—*Vitamin and Mineral Content of the Test Food*

Ingredient	Calculated Amount Added per Can	Amount per Can Determined by Analysis
Vitamin A.....	1,500 U. S. P. units	2,480 U. S. P. units
Vitamin D.....	500 U. S. P. units	500 U. S. P. units
Vitamin B ₁	1,000 micrograms	1,070 micrograms
Vitamin C.....	120 mg.	86 mg.
Vitamin B ₆	1,500 micrograms	3,600 micrograms
Biotin.....	None	15.2 micrograms
Pantothenic acid.....	None	3,083 micrograms
Iron.....	10 mg.	9.3 mg.
Copper.....	2 mg.	4.4 mg.
Manganese.....	2 mg.	1.23 mg.

Keeping Quality.—The product has been found to remain unchanged for six months, the average shelf life of most proprietary products. The average composition given in table 1 is that found at the end of this period.

Preservation of Vitamin C.—Since vitamin C is the most easily destroyed of all the ingredients, a special table is attached to show the rate of destruction of this vitamin during storage (table 2). A table is also presented to show the content of vitamin C in a typical formula made by diluting the concentrated food with water and storing it for twenty-four hours in a refrigerator, a custom practiced by almost every mother (table 3).

TABLE 2.—*Data Showing Influence of Storage at Room Temperature on Vitamin C Content of a Food for Infants, Manufactured under Commercial Conditions*

Sample Number	Vitamin C per 13 Fluidounce (14½ Ounce) Can by Titration		
	Freshly Made (1 Week After Preparation) Mg. per Can	Stored at Room Temperature	
		Time of Storage, Months	Mg. per Can
8	101	3	93
11C30	100	4	95
1011	62	12	57

The analytic methods used for the determination of the amounts of various vitamins in the baby food were as follows: For the determination of vitamin A the extracted oil was examined in a Bills and Wallenmeyer electronic photometer which had been previously standardized with U. S. P. reference cod liver oil.¹ The content of vitamin C was determined both biologically,² as a preventive of symptoms of de-

1. Bills, C. E., and Wallenmeyer, J. C.: A Photoelectric Photometer for Vitamin A Determinations, *J. Biol. Chem.* **123**:xi, 1938.

2. Sherman, H. C., and Smith, S. L.: The Vitamins, ed. 2, New York, Chemical Catalog Company, 1931.

ficiency in guinea pigs, and chemically by titration with 2, 6-dichlorophenolindophenol. The method of Bessey and King³ was used for the titration except that a mixed solution containing 10 per cent acetic acid with 4 per cent phosphoric acid was used instead of trichloroacetic acid. The yeast fermentation method described by Schultz, Atkin and Frey⁴ was used for thiamine, and microbiologic methods were used for the determination of the contents of riboflavin,⁵ nicotinic acid⁶ and pantothenic acid.⁷ Vitamin D⁸ was assayed by the U. S. P. method as modified for testing milk.

TABLE 3.—*Vitamin C Content of a Typical Formula Made from the Test Food*

Sample No.	Description of Sample	Vitamin C by Titration, Mg. per Qt.		
		Freshly Prepared	After 6 Hr. at 40 F.	After 24 Hr. at 40 F.
1	Infant food undiluted; can opened and product stored in bottles.....	148	134	131
2	5 fluidounces (148 cc.) infant food, 6 fluidounces (177 cc.) water* and 1 tbsp. corn syrup (15 cc.)†, mixed and bottled cold	60	56	52
3	5 fluidounces infant food, 6 fluidounces water* and 1 tsp. sugar (5 cc.), mixed and bottled cold	68	63	54
4	Same ingredients as no. 2, but mixed and bottled hot and cooled to 40 F.	75	70	66

* Tap water, boiled and cooled.

† Blue Label Karo Syrup.

PRACTICAL USE

The purpose of this study was to demonstrate that a complete food for infants such as that

3. Bessey, O. A., and King, C. G.: Distribution of Vitamin C in Plant and Animal Tissues, and Its Determination, *J. Biol. Chem.* **103**:687, 1933.

4. Schultz, A. S.; Atkin, L., and Frey, C. N.: A Fermentation Test for Vitamin B₁, *J. Am. Chem. Soc.* **59**:948, 1937; A Fermentation Test for Vitamin B, *ibid.* **59**:2457, 1937; The Specificity of the Fermentation Test for Vitamin B, *ibid.* **60**:3084, 1938. Schultz, A. S.; Atkin, L.; Frey, C. N., and Williams, R. R.: Application of the Sulfite Cleavage of Thiamin to the Yeast Fermentation Method, *ibid.* **63**:632, 1941. Atkin, L.; Schultz, A. S., and Frey, C. N.: Ultramicrodetermination of Thiamine by Fermentation Method, *J. Biol. Chem.* **129**:471, 1939.

5. Snell, E. E., and Strong, F. M.: A Microbiological Assay for Riboflavin, *Indust. & Engin. Chem. (Anal. Ed.)* **11**:346, 1939.

6. Snell, E. E., and Wright, L. D.: Microbiological Method for Determination of Nicotinic Acid, *J. Biol. Chem.* **139**:675, 1941.

7. Pennington, D.; Snell, E. E., and Williams, R. J.: Assay Method for Pantothenic Acid; *J. Biol. Chem.* **135**:213, 1940.

8. Skinner, W. W., and others: Official and Tentative Methods of Analysis of the Association of Official and Agricultural Chemists, ed. 5, Washington, D. C., The Association, 1940, pp. 282-286.

described in the first part of this paper would support normal growth and development and would prevent vitamin deficiencies in infants.

Experimental Subjects.—One hundred and one healthy infants up to 2 months of age were chosen for study. Of this number 83, 82 per cent, remained under satisfactory observation for a period sufficiently long to justify classification of their records as complete.⁹ Seventy-five of these were provided by the well baby clinics of the Bureau of Child Hygiene of the Baltimore City Health Department and the Babies Milk Fund Association and 5 by a home for orphans; 3 were private patients. There were 49 white and 34 Negro subjects. Forty-four were boys and 39 were girls. The youngest infant in the series began to take the test food during its first week of life. The study was not continued for any infant who had attained the age of 9 months. Clinics were chosen in a variety of neighborhoods so as to provide a fair cross section of economic levels.

Procedure.—It was originally planned that throughout the period of study the subjects should receive only the test food with added carbohydrate. This plan was carried out until the infants reached the age of 6 months, when it became obvious that the mothers would be greatly tempted to add solid food of some type against advice. It was felt that the addition of plain, bleached cereal, free of supplementary vitamins, at this time might discourage the promiscuous use of other foods. All tests for the components of the vitamin B complex were carried out before it was added to the diet. This policy had favorable results.

The test food was distributed in cans containing 13 fluidounces. The feedings provided from 50 to 60 calories per pound (about 120 calories per kilogram) per day. The amount of carbohydrate added, in the form of cane sugar or corn syrup, varied between 5 and 10 per cent of the total bulk of the formula. This was accomplished by the addition of approximately 1 ounce (28 Gm.) of sugar or of syrup for each 6 to 8 ounces (175 to 235 cc.) of the test food. The carbohydrate was supplemented rather than included in the test food. This was done, first, because it was felt that the food could be considered complete without this added carbohydrate and, second, because if added carbohydrate should be desired it could be supplied as a supplement in quantities calculated to produce the protein-carbohydrate ratio suitable for the individual infant. The ratio of food to water varied from 1:1 to 1:2. Thus, within certain definite limits, variations to fit the needs of the individual baby were allowed. The administration of any supplementary vitamins was specifically forbidden. In only 1 instance did the amount of test milk used daily exceed the content of a can (13 fluidounces). The purpose of limiting infants to one can a day was mainly to simplify the problem of distribution, but the limitation also served to standardize the quantity of food consumed.

9. The records of 18 of the 101 infants accepted for study were discarded, in 7 instances because of poor cooperation or the proof that the parents were unreliable and in 7 because the families of the infants left the city during the first few months of the study. Two infants were fatally burned after only two months of observation; 1 infant died of pertussis early in the period of study, and 1 infant had pneumonia complicated by empyema during the first two months of study and was excluded from the group to be studied because of the extended course of the illness.

The babies were examined by the same physician at monthly intervals or more frequently when it seemed advisable. Weights and detailed measurements were taken.

The study was carried out over a period of one year. The plan called for a six month period of observation for each subject; however, 1 infant was studied for only three and a half months and 5 infants for four and a half months. In these instances complete roentgen and clinical studies were obtained. The remaining 77 infants were followed for not less than five months. The longest period of observation was eight months, and the average period of study for the whole group was five and eight-tenths months.

Attempted Safeguards: In any study of this kind the questions arise, first, whether the infants actually received the recommended food and, second, whether additional foods and vitamin-containing substances were administered. In this study an attempt to approximate total cooperation within the limit of human possibilities was made in the following manner:

A full time, trained social worker gave her undivided attention to the close supervision of the subjects. Each infant was examined and the parent questioned by the physician at intervals of four weeks or less. The social worker visited the home or otherwise made contact with the family at a time midway between the visits to the clinic. Each infant was chosen after a full inquiry into the economic status and reliability of the parents, the nature of the home conditions and the general environmental factors. An effort was made, apparently with success, to establish good rapport between the social worker and the family. The worker rendered assistance in ways not directly connected with the study.

Cans of food were supplied in lots sufficient for two weeks only, and the parent was thus brought back to the clinic for more frequent contact with the worker, who personally distributed the food. Printed material emphasizing the requirements of the study was distributed. The saving of expense was pointed out. Each parent was assured that the food contained adequate vitamins and that additional vitamins would be excessive.

Results.—In the opinion of the examiner and of all other observers the subjects thrived and constituted a group of robust and vigorous infants. Even those who when first seen presented unfavorable nutritional features did well. No clinical evidence of any vitamin deficiency was observed. The feedings evidently were palatable and were well taken.

WEIGHT: The average weight of 80 infants at 5 months of age was 15.6 pounds (about 7,000 Gm.) (standard, 15.6 pounds). At 6 months the average for 70 infants was 16.9 pounds (about 7,700 Gm.) (standard, 16.5

10. The standards for comparison of weight and height are taken from the tables computed by Dr. W. C. Davison in *The Compleat Pediatrician*, ed. 4, Durham, N. C., Duke University Press, 1943. These figures were compiled from a number of sources, including *The Growth and the Development of the Baby* by Morris Stark, *Endocrine Medicine* by William Engelbach and the *Weight-Height-Age Tables of the Bureau of Education*, Department of the Interior, Washington, D. C.

pounds [7,485 Gm.]). At 7 months the average for 43 infants was 18.0 pounds (8,200 Gm.) (standard, 17.6 pounds [3,000 Gm.]). For 16 infants 8 months of age the average weight was 18.9 pounds (8,570 Gm.) (standard, 18.75 pounds [8,500 Gm.]).

The average gain in weight for 78 infants from birth to the age of 3 months was 7.9 ounces (225 Gm.) per week (standard, 7.75 ounces [220 Gm.]). The average for 80 subjects during the second trimester was 5.4 ounces (150 Gm.) per week (standard, 5.0 ounces [140 Gm.]). For 22 subjects during the third trimester, between the ages of 6 and 9 months, the average gain was 4.3 ounces (120 Gm.) per week (standard, 3.25 ounces [95 Gm.]).

HEIGHT¹⁰: Measurements were taken at monthly intervals, but only those made when the infants were 5 and 6 months of age are presented. Seventy-six babies measured at 5 months had an

TABLE 4.—*Weight and Height of Subjects*

	Number of Subjects	Average for Subjects Studied	Normal Values
Weight at 5 months.....	80	15.6 lb.	15.6 lb.
Weight at 6 months.....	70	16.9 lb.	16.6 lb.
Weight at 7 months.....	43	18.0 lb.	17.6 lb.
Weight at 8 months.....	16	18.9 lb.	18.75 lb.
Average gain, 0-3 months....	78	6.9 oz. per wk.	6.75 oz. pr wk.
Average gain, 3-6 months....	80	5.4 oz. per wk.	5.0 oz. pr wk.
Average gain, 6-9 months....	22	4.3 oz. per wk.	3.2 oz. pr wk.
Height at 5 months.....	76	25.8 in.	25.0 in.
Height at 6 months.....	71	26.2 in.	26.1 in.

average height of 25.8 inches (65.5 cm.) (standard, 25.0 inches [63 cm.]). Seventy-one infants at the age of 6 months had an average length of 26.2 inches (66.3 Gm.) (standard, 26.1 inches [66.1 cm.]).

HEMOGLOBIN: The amount of hemoglobin, determined by the Sahli method, in the blood of 18 subjects averaged 11.5 Gm. per hundred cubic centimeters.

ROENTGENOGRAMS: Roentgenologic studies were completed for 75 of the 83 subjects, and in no instance was any evidence of rickets or scurvy demonstrated. The diagnoses presented by the roentgenologists were reviewed by Dr. E. A. Park and by the physician conducting the study.

SERUM CALCIUM: Determinations of the serum calcium carried out by the method of Kramer and Tisdall for 42 infants in the last month of the period of study gave an average of 10.2 mg. per hundred cubic centimeters. The normal figures generally quoted lie between 9.0 and 11.0 mg. The highest value was 13.7, the lowest 8.3 and the second lowest 9.0 mg.

SERUM PHOSPHORUS: The average of 4 determinations of serum phosphorus by the method of Fiske and Subbarow was 7.0 mg. per hundred cubic centimeters. The generally quoted normal lies between 5.0 and 6.0 mg. The highest value was 8.8, the lowest 3.9 and the next lowest 5.2 mg.

SERUM PHOSPHATASE: Determinations of the phosphatase activity of the serum of 42 infants by a modification of the method of Bodansky gave an average of 17 Bodansky units per hundred cubic centimeters. The results varied widely and seemed to bear no definite relationship to the levels of calcium or phosphorus or to the roentgenographic appearances.

VITAMIN C: Determinations obtained for 4 infants by the method of Mindlin and Butler¹¹ gave an average of 0.88 mg. of vitamin C per hundred cubic centimeters of blood. The highest value was 1.33, the lowest 0.41 and the next lowest 0.51 mg. The normal range according to Dr. Laslo Kajdi, who performed the test, lies between 0.5 and 1.0 mg. A higher average figure, in the neighborhood of 1.0 mg. per hundred cubic centimeters, was anticipated until the last 8 specimens were presented. The values for this entire group were considerably lower than the previous average but were well within the normal limits. Dr. Kajdi suggested that the deviation might well have been due to an error in the method of determination.

VITAMIN A: Tests for carotene and vitamin A in the blood were carried out by the Josephs modification of the method of Clause and McCoord.¹² The average of 16 determinations of vitamin A was 96 units per hundred cubic centimeters (normal 50 to 150 units). The greatest value was 155 and the lowest 60 units.

THIAMINE: Twenty-nine analyses of the urine for thiamine by the method of Hennessy and Cerecedo¹³ gave an average of 13.6 microgram (normal 0.06 to 10.0 micrograms) per hundred cubic centimeters. The highest value was 33.4, the lowest 0.63 and the second lowest 5.3 micrograms.

RIBOFLAVIN: For 9 specimens of urine analyzed by the fluorometric method of Najjar¹⁴

11. Mindlin, R. W., and Butler, A. M.: The Determination of Ascorbic Acid in Plasma: A Macromethod and Micromethod, *J. Biol. Chem.* **122**:673, 1938.

12. Josephs, H. W.: Studies in Vitamin A, *Bull. Johns Hopkins Hosp.* **65**:112, 1939.

13. Hennessy, D. J., and Cerecedo, L. R.: The Determination of Free and Phosphorylated Thiamine by a Modified Thiochrome Assay, *J. Am. Chem. Soc.* **61**:179, 1939.

14. Najjar, V. A.: The Fluorometric Determination of Riboflavin in Urine and Other Biological Fluids, *J. Biol. Chem.* **141**:355, 1941.

the average of the results was 64.5 micrograms of riboflavin per hundred cubic centimeters (normal 2.0 to 15.0 micrograms). The highest value was 155.0, the lowest 3.3 and the second lowest 25.6 micrograms.

These values in particular, as well as those for other components of the vitamin B complex, are considered to be high.

F_2 (N-methylnicotinamide derivative): By a modification¹⁵ of the method of Najjar and Wood,¹⁶ determinations were made of the amounts of the derivative of nicotinamide described by the author in the urine of 10 subjects. The average excretion of F_2 expressed as N-methylnicotinamide chloride¹⁶ equaled 266 micrograms (normal 34 to 350 micrograms) per hundred cubic centimeters. The highest was equivalent to 838, the lowest to 62 and the second lowest to 82 micrograms of N-methylnicotinamide chloride.

Acute Illnesses and Other Modifying Factors.—It was felt that the 22 acute illnesses which

ticularly beset by acute infections. The question of separating these figures from those of the main study, as invalid, was considered, but this was not done.

PREMATURE INFANTS

No premature infants were studied. The test food contained an inflexible proportion of vitamins, and in view of the relatively small amount of food required by small premature infants it was felt that this type of feeding unless supplemented by the administration of additional vitamins was not to be recommended.

TREATMENT OF SCURVY

One infant of 10 months with active scurvy was treated by the administration of the test food alone, in the usual quantities. Clinical improvement was observed in two to three days. Roentgenologic evidence of healing was noted at the end of one week, and advanced healing was observed at the end of the second week.

TABLE 5.—*Chemistry of the Blood and Urine*

	Number of Determinations	Average for Subjects Studied	Highest Value	Lowest Value	Second Lowest Value	Normal Values
Calcium, mg./100 cc. of blood.....	45	10.2	13.7	8.3	9.0	9.0-11.0
Phosphorus, mg./100 cc. of blood.....	45	7.0	8.8	5.2	5.2	5.0-8.0
Phosphatase, Bodansky units/100 cc. of blood..	45	17.0	65.5	2.6	8.0	5.0-7.0
Vitamin C, mg./100 cc. of blood.....	45	0.88	1.33	0.41	0.51
Vitamin A, units/100 cc. of blood.....	16	98	160	60	75	50-150
Thiamine, mg./100 cc. of urine.....	29	0.0372	0.0668	0.0021	0.0106	0.002-0.020
Riboflavin, mg./100 cc. of urine.....	9	0.135	0.310	0.0366	0.0512	0.005-0.080
F_2 as N-methylnicotinamide chloride, mg./100 cc. of urine	10	0.266	0.898	0.062	0.082	0.034-0.350

occurred in the 83 infants were tolerated well. The use of the test food was continued throughout the illnesses. Diarrheal episodes of short duration were observed in 12 infants and in practically all instances were shown to be related to parenteral infection. Seven infants had pneumonia; 5 had purulent otitis media; 4 had pertussis; 3 had generalized furunculosis; 2 had chickenpox and 1 had measles. Constipation of any severity was infrequent and responded ordinarily to the administration of prune juice, which was permitted. An almost unprecedented period of extreme heat during the last two months of the study (June and July, 1943) undoubtedly affected the average gain in weight. The infants at the home for orphans were par-

SUMMARY

Eighty-three infants received a test food consisting of complete, supplemented evaporated milk for an average of six months. The infants thrived, and the weights and measurements for the group compared favorably with accepted standards. No clinical or roentgenologic evidence of vitamin deficiency was observed, and chemical analyses of the blood and urine gave no indication of vitamin deficiency. The normal processes of digestion and elimination were not disturbed in any discernible manner.

CONCLUSIONS

It is concluded that the test food described is a suitable complete food for infants for at least the first nine months of life, that this food will support normal growth and development and that it will prevent vitamin deficiency.

The food is well adapted to transportation, storage and distribution.

Miss Anice Sampson contributed to this study in her capacity as the social worker.

615 North Wolfe Street.
1011 North Charles Street.

15. Najjar, V. A.: The Laboratory Diagnosis of Nicotinic Acid Deficiency: An Improved Procedure for the Determination of F_2 (N-Methylnicotinamide Derivative) in Urine, *Bull. Johns Hopkins Hosp.* **74**: 392, 1944.

16. Najjar, V. A., and Wood, R. W.: Presence of a Hitherto Unrecognized Nicotinic Acid Derivative in Human Urine, *Proc. Soc. Exper. Biol. & Med.* **44**: 386, 1940.

BACTERICIDAL ACTION OF PENICILLIN ON BACTERIA COMMONLY PRESENT IN INFECTIONS OF URINARY TRACT

WITH ESPECIAL REFERENCE TO STREPTOCOCCUS FAECALIS

HENRY F. HELMHOLZ, M.D.*

AND

CHIEH SUNG, M.D., D.P.H.

Assistant in Pediatrics, the Mayo Clinic

ROCHESTER, MINN.

Since the advent of chemotherapy in the management of infections of the urinary passages, several milestones in its progress can be marked. As recently as 1895, when Nicolaier first instituted the use of methenamine for patients with such infections, the treatment consisted of alkalinization when the urine was acid and acidification when it was alkaline. In 1931, the ketogenic diet was introduced, and betaoxybutyric acid produced physiologically by the body gave urine definite bactericidal properties when its acidity ranged between p_H 5 and 5.5. The difficulty of management and the lack of economy of the ketogenic diet have been obvious, and Rosenheim's introduction of mandelic acid in place of betaoxybutyric acid was a great step forward. However, mandelic acid in large amounts is likely to cause digestive upset and occasional hematuria. Furthermore, when the kidneys are damaged or when the infection is one of those producing a persistent strongly alkaline reaction of the urine, the necessary concentration of the organic acid or a sufficiently low p_H or both cannot be reached, and the effectiveness of mandelic acid is thus limited. With the introduction of sulfonamide compounds urinary antisepsis became greatly simplified. In concentrations that can be easily reached in urine, sulfonamide compounds prove bactericidal for all bacteria found in persons with infections of the urinary passages with the exception of *Streptococcus faecalis*. For the latter an acidity of p_H 5.5 or less in urine has to be maintained if any efficacy is to be expected. Thus if a patient with infection of the urinary passages due to *Str. faecalis* has damaged kidneys and therefore cannot excrete urine with a sufficiently low p_H value, therapy with a sulfonamide compound is ineffective. It was with this type of patient in mind that we undertook to determine the effect of penicillin on *Str. faecalis* in urine.

Relatively little work has been done on the effect of penicillin on *Str. faecalis*, particularly on strains isolated from persons with infections of

the urinary tract. Bornstein¹ stated that all of his 27 strains of enterococci proved to be resistant to penicillin in a concentration of 8 of his units per cubic centimeter of broth. Fleming² in his original article placed the resistance of *Str. faecalis* to penicillin in the same category as that of the colon-typhoid group of gram-negative bacilli. McKee and Rake³ put *Str. faecalis* in the group with Friedländer's bacillus, *Salmonella* and *Aerobacter aerogenes*, which they found are not susceptible to penicillin. Fisher,⁴ in an extensive report on antibacterial properties of crude penicillin, labeled 5 strains of alpha *Str. faecalis* as the resistant organisms. Furthermore, we cannot as yet find, in a search of the literature, any detailed study of the bactericidal action of penicillin on bacteria commonly present in the infections of the urinary passages, including the gram-negative bacilli as well as *Str. faecalis* and *Staphylococcus aureus*.

METHOD OF STUDY

We had available for study 30 strains of *Str. faecalis*, 13 strains of *Proteus ammoniae*, 39 strains of *Escherichia coli*, 18 strains of *A. aerogenes*, 3 strains of *Pseudomonas aeruginosa* and 11 strains of *Staph. aureus*. All these organisms were originally isolated from urine of patients with infections of the urinary tract. These stock cultures were kept on agar slant at a temperature of 4 C. The 2 samples of urine used in these experiments were collected from patients receiving penicillin for coccic infections and contained 30 and 60 Oxford units per cubic centimeter respectively. The urine was Seitz-filtered, and a test for sterility was carried out on the filtrate before each series of experiments.

1. Bornstein, S.: Action of Penicillin on Enterococci and Other Streptococci, *J. Bact.* **39**:383-387 (April) 1940.

2. Fleming, A.: On the Antibacterial Action of Cultures of Penicillium, with Special Reference to Their Use in the Isolation of B. Influenzae, *Brit. J. Exper. Path.* **10**:226-236 (June) 1929.

3. McKee, C. M., and Rake, G.: Biological Experiments with Penicillin, *J. Bact.* **43**:645 (May) 1942.

4. Fisher, A. M.: The Antibacterial Properties of Crude Penicillin, *Bull. Johns Hopkins Hosp.* **73**:343-378 (Nov.) 1943.

* Section on Pediatrics, the Mayo Clinic.

In each experiment a fresh twenty-four hour culture of each organism in a special brain broth was employed. The reaction was adjusted to p_H 7.6. This special brain broth had the advantage of giving a rich and uniform growth throughout the tube to all the common organisms on incubation at 37 C. for twenty-four hours. Five cubic centimeter portions of the samples of urine were pipetted into the sterile test tubes. Only a minute quantity of the special brain broth culture of each organism was used to inoculate the sample of urine by dipping an average-sized platinum wire into the broth culture to a depth of 4 mm. The tube was thoroughly shaken and the urine sucked up into the pipet repeatedly, and 0.5 cc. of the inoculated urine was immediately plated with warm agar, as little time as possible being left between the inoculation and the plating. These plates were incubated for twenty-four to forty-eight hours; at the end of the period of incubation the colonies were counted, and the numbers were recorded in the tables herein presented, in the column headed "Immediately After Inoculation." The inoculated samples of urine in the test tubes were incubated at 37 C. for twenty-four hours. After twenty-four hours' incubation, 0.5 cc. of the urine was again removed from the test tube and was plated with agar. The plate was likewise incubated for twenty-four to forty-eight hours. The number of colonies counted on each plate then was entered in the column "After Twenty-Fours Hours' Incubation" in the tables. When the count exceeded 20,000 colonies per plate, it was put down as "innumerable."

RESULTS

1. *Str. Faecalis*.—Table 1 shows that urine containing 4 Oxford units of penicillin per cubic

TABLE 1.—The Effect of Penicillin on Six New Strains of *Str. Faecalis* with Respect to Amounts of Inoculation of Organisms into Urine Containing 4 Oxford Units per Cubic Centimeter

Strain	Number of Bacteria in 0.5 Cc. of Urine			
	Light Inoculation		Heavy Inoculation	
	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation
A1	3,790	40	12,000	1,560
A2	5,985	123	Innumerable	6,240
A3	2,330	24	11,220	15
A4	598	5	1,200	13
A5	1,463	3	4,980	2
A6	3,125	24	12,300	4

centimeter had definite bactericidal effect on 6 freshly isolated strains of *Str. faecalis*. With routine relatively light inoculations the reduction was from thousands of bacteria per 0.5 cc. of urine immediately after inoculation of the organism to 123 or less per 0.5 cc. of urine after twenty-four hours' incubation. When the inoculations consisted of single loopfuls of the brain broth culture of the organism, the final counts of bacteria were also sharply reduced.

As is shown in table 2, there was considerable reduction of the numbers of bacteria after twenty-four hours' incubation at 3 units per cubic centimeter. There were slight inhibition in 3 of the 6 strains at 2 units per cubic centimeter and marked growth of the other 3 strains.

At 1 unit per cubic centimeter there was marked growth of all the strains.

With concentrations of 30, 15, 8 and 6 Oxford units of penicillin per cubic centimeter of urine there were a marked reduction of the number of

TABLE 2.—The Effect of Varying Lower Concentrations of Penicillin on the Inhibition of Growth of *Str. Faecalis*

Strain	Number of Bacteria in 0.5 Cc. of Urine					
	3 Oxford Units per Cc.		2 Oxford Units per Cc.		1 Oxford Unit per Cc.	
	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation
A1	4,680	137	2,640	Innumerable	1,600	Innumerable
A2	9,120	900	7,680	Innumerable	5,700	Innumerable
A3	2,400	52	1,560	Innumerable	1,100	Innumerable
A4	228	4	480	9,300	50	4,200
A5	1,500	90	630	3,240	1,020	Innumerable
A6	5,100	33	1,020	2,640	2,220	Innumerable

bacteria in the first six hours of incubation in all dilutions and a comparatively small reduction in the next eighteen hours (table 3). This result agrees with the findings of Hobby, Meyer and Chaffee⁵ in their studies on penicillin. They found that there is a geometric decrease

TABLE 3.—The Effect of Varying Higher Concentrations of Penicillin in Urine on Inhibition of Growth of *Str. Faecalis*

Strain	Number of Bacteria in 0.5 Cc. of Urine							
	30 Oxford Units per Cc.		15 Oxford Units per Cc.		8 Oxford Units per Cc.		6 Oxford Units per Cc.	
	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation
A1	1,260	0	3,600	2	4,250	2	Innumerable	11
A2*	3,300	2	Innumerable	108	Innumerable	280	Innumerable	58
A3	1,800	0	1,250	3	2,300	3	3,210	2
A4	2	0	19	0	22	13	226	0
A5	600	2	606	0	1,800	0	1,350	0
A6	3,780	3	4,200	42	5,400	33	Innumerable	5

* After six hours showed 480 colonies in urine containing 15 units per cubic centimeter, 720 colonies in urine containing 8 units per cubic centimeter and 1,380 colonies in urine containing 6 units per cubic centimeter.

of the number of bacteria with an arithmetical increase of time.

As is recorded in table 4, 24 old strains of *Str. faecalis* were tested with penicillin in a con-

5. Hobby, G. L.; Meyer, K., and Chaffee, E.: Observations on the Mechanism of Action of Penicillin, Proc. Soc. Exper. Biol. & Med. 50:281-285 (June) 1942.

centration of 4 Oxford units per cubic centimeter of urine. There was a marked bactericidal effect on all of them but no complete killing off of any of these strains, although counts as low as 2, 9 and 13 per 0.5 cc. of urine were observed after twenty-four hours' incubation when the initial inoculations were 660, 1,380 and 480 Oxford units per 0.5 cc. of urine

TABLE 4.—*The Effect of Penicillin in Urine (4 Units per Cubic Centimeter) on 24 Old Strains of Streptococcus Faecalis*

Strain	Number of Bacteria in 0.5 Cc. of Urine	
	Immediately After Inoculation	After 24 Hours' Incubation
4.....	2,520	660
6.....	6,300	420
10.....	1,380	9
11.....	3,600	84
12.....	2,520	82
14.....	3,720	100
15.....	2,400	40
21.....	2,760	540
22.....	4,320	288
23.....	660	2
24.....	2,580	116
25.....	2,820	180
26.....	1,080	156
27.....	3,240	48
28.....	900	27
29.....	2,340	90
30.....	1,080	27
31.....	3,900	57
33.....	480	13
34.....	3,720	360
35.....	9,000	89
36.....	4,860	120
37.....	3,660	36
38.....	3,120	109

respectively. In view of the low level of 3 units per cubic centimeter at which *Str. faecalis* is markedly reduced in number, the higher concentrations of penicillin that can easily be reached

and his co-workers⁶ in that this organism proved relatively vulnerable to the action of penicillin. As is shown in table 5, at a concentration of 30 Oxford units per cubic centimeter of urine there was bactericidal effect on all 13 strains. After twenty-four hours there was no growth with

TABLE 5.—*The Effect of Penicillin on 39 Strains of Escherichia Coli in Urine Containing 30 Oxford Units per Cubic Centimeter*

Strain	Number of Bacteria in 0.5 Cc. of Urine	
	Immediately After Inoculation	After 24 Hours' Incubation
1.....	2,100	0
2.....	5,700	Innumerable
3.....	5,760	1
5.....	3,540	144
6.....	5,400	Innumerable
7.....	4,200	Innumerable
8.....	5,220	Innumerable
9.....	7,920	134
10.....	5,100	Innumerable
11.....	3,300	Innumerable
12.....	3,240	Innumerable
13.....	1,500	0
14.....	3,000	42
15.....	3,780	0
16.....	3,960	Innumerable
17.....	3,960	9,060
18.....	2,520	Innumerable
19.....	2,960	0
20.....	4,200	44
21.....	6,420	Innumerable
23.....	4,020	123
24.....	5,580	Innumerable
25.....	6,000	Innumerable
26.....	4,800	4
27.....	4,500	Innumerable
28.....	9,180	Innumerable
29.....	9,780	15,000
30.....	6,960	40
31.....	3,030	1
32.....	5,760	3
33.....	6,630	Innumerable
34.....	2,700	Innumerable
35.....	7,680	Innumerable
36.....	6,660	1
37.....	4,020	Innumerable
38.....	4,800	Innumerable
40.....	2,680	4,560
41.....	1,980	0
42.....	3,900	Innumerable

TABLE 5.—*The Effect of Various Concentrations of Penicillin in Urine on 13 Strains of Proteus Ammoniae*

Strain	Number of Bacteria in 0.5 Cc. of Urine									
	30 Oxford Units per Cc.		15 Oxford Units per Cc.		8 Oxford Units per Cc.		4 Oxford Units per Cc.		3 Oxford Units per Cc.	
	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation
1.....	4,800	117	1,980	3	9,000	780	6,120	Innumerable
2.....	3,300	68	4,560	169	18,900	720	6,660	Innumerable
3.....	3,420	1	1,200	4	2,100	14	2,340	12	1,500	Innumerable
4.....	2,880	0	3,360	1,890	1,860	Innumerable	3,960	1,080	400	Innumerable
6.....	8,100	0	3,840	22	2,820	133	6,360	Innumerable
7.....	2,400	240	6,480	720	3,000	840	3,240	Innumerable
8.....	1,080	22	1,680	12	3,240	24	2,160	Innumerable
9.....	5,400	3	1,740	102	2,700	10	2,940	1,080	9	Innumerable
11.....	1,200	1	1,500	38	1,680	57	2,220	600	3,000	Innumerable
13.....	1,140	0	6,720	3,640	12,480	Innumerable	6,000	Innumerable
14.....	2,160	1	2,520	27	2,400	27	2,940	Innumerable
15.....	5,940	2	8,660	1,680	2,580	133	2,580	Innumerable
16.....	3,000	1	1,860	88	1,320	0	1,140	6	900	Innumerable

in the urine and the presence of the natural defense mechanism of the human organism, it would seem that penicillin should prove useful in combating this infection in clinical cases.

2. *P. Ammoniae*.—Our conclusions on *P. ammoniae* were in agreement with those of Florey

3 strains and only 1 colony with 4 strains. Only 2 of the 6 remaining strains showed more than

6. Abraham, E. P.; Chain, E.; Fletcher, C. M.; Gardner, A. D.; Heatley, N. G.; Jennings, M. A., and Florey, H. W.: Further Observations on Penicillin, *Lancet* 2:177-188 (Aug. 15) 1941.

00 colonies: 117 and 240 respectively. At 15 units per cubic centimeter there was definite inhibition of all of the strains. At 8 units per cubic centimeter the inoculation ranged from 3,200 to 18,900 per 0.5 cc., and the cultures after twenty-four hours' incubation showed

TABLE 7.—The Effect of Higher Concentrations of Penicillin in Urine on 23 Relatively Resistant Strains of *Escherichia Coli* (see table 6)

Strain	Number of Bacteria in 0.5 Cc. of Urine			
	60 Oxford Units per Cc.		45 Oxford Units per Cc.	
	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation
2	5,430	Innumerable	7,320	Innumerable
6	4,590	111	4,620	Innumerable
7	4,080	Innumerable	7,920	Innumerable
8	7,280	Innumerable	5,820	Innumerable
10	5,400	Innumerable	3,180	Innumerable
11	4,200	23	4,680	Innumerable
12	6,240	53	4,200	Innumerable
16	5,100	Innumerable	4,920	Innumerable
17	7,260	350	5,460	Innumerable
18	3,120	Innumerable	5,400	Innumerable
21	3,660	Innumerable	7,660	Innumerable
24	4,260	Innumerable	13,620	Innumerable
25	4,560	Innumerable	4,620	Innumerable
27	4,520	Innumerable	5,640	Innumerable
28	6,000	Innumerable	19,920	Innumerable
29	4,500	Innumerable	5,220	Innumerable
33	3,420	Innumerable	5,460	Innumerable
34	8,460	Innumerable	10,260	Innumerable
35	5,460	Innumerable	5,820	Innumerable
37	1,980	15	3,000	Innumerable
38	4,380	Innumerable	5,340	Innumerable
40	6,360	Innumerable	6,480	Innumerable
42	6,840	Innumerable	11,880	Innumerable

marked increase in only 2 strains, counts between 700 and 900 with 3 strains and counts of 133 or less with the remaining 8 strains. At 4 units per cubic centimeter 5 of the 13 strains were inhibited, and these 5 strains grew out to innumerable

cubic centimeter of urine (table 6). At this concentration 16 strains exhibited inhibition of growth, 5 were completely killed off, 5 showed fewer than 5 colonies and in the remaining 6 the highest count was 144. After this preliminary experiment the 23 relatively resistant strains were subjected to tests with 45 and 60 Oxford units per cubic centimeter of urine (table 7). They all grew to innumerable with 45 units per cubic centimeter, but 5 strains were inhibited at 60 Oxford units per cubic centimeter, showing a decrease in number from the usual initial counts in the thousands to from 15 to 350 colonies after twenty-four hours' incubation. With the 16 relatively susceptible strains the effect of lower concentrations of penicillin in urine was tried out (table 8). At 15 units per cubic centimeter 3 strains were still inhibited, but at 8 and 4 units per cubic centimeter all 16 strains grew to innumerable. Of these 39 strains of *Escherichia coli*, only 21 (54 per cent) were inhibited at 60 units per cubic centimeter, 16 (41 per cent) at 45 and 30 units per cubic centimeter, 3 (8 per cent) at 15 units per cubic centimeter and none at 8 units per cubic centimeter.

4. *A. Aerogenes*.—Table 9 is a composite chart of a series of experiments carried out on the 18 strains of *A. aerogenes*. At a concentration of 30 Oxford units of penicillin per cubic centimeter of urine 2 (11 per cent) of the 18 strains were inhibited, but both these strains grew to innumerable at 15 Oxford units per cubic centimeter. The other 16 strains (89 per cent) grew to innumerable at 30 units per cubic

TABLE 8.—The Effect of Lower Concentrations of Penicillin in Urine on 16 Relatively Susceptible Strains of *Escherichia Coli* (see table 6)

Strain	Number of Bacteria in 0.5 Cc. of Urine					
	15 Oxford Units per Cc.		8 Oxford Units per Cc.		4 Oxford Units per Cc.	
	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation
1	1,500	0	1,440	Innumerable	1,740	Innumerable
3	4,080	Innumerable	2,280	Innumerable	4,980	Innumerable
5	1,440	Innumerable	2,100	Innumerable	2,400	Innumerable
9	1,920	2	1,320	Innumerable	2,460	Innumerable
13	1,320	Innumerable	1,260	Innumerable	1,200	Innumerable
14	2,460	Innumerable	2,040	Innumerable	2,520	Innumerable
15	1,500	Innumerable	1,980	Innumerable	4,200	Innumerable
19	1,320	Innumerable	3,000	Innumerable	2,460	Innumerable
20	2,220	Innumerable	2,400	Innumerable	1,380	Innumerable
23	960	Innumerable	1,560	Innumerable	1,080	Innumerable
25	3,420	Innumerable	1,500	Innumerable	3,240	Innumerable
30	3,480	Innumerable	3,480	Innumerable	4,980	Innumerable
31	3,120	Innumerable	7,260	Innumerable	4,920	Innumerable
32	1,920	Innumerable	1,620	Innumerable	3,300	Innumerable
36	2,580	103	3,600	Innumerable	4,680	Innumerable
41	1,920	Innumerable	3,180	Innumerable	6,600	Innumerable

ble at 3 units per cubic centimeter. Thus at 8 units per cubic centimeter a definite reduction of the number of *P. ammoniae* organisms was brought about in twenty-four hours.

3. *Esch. Coli*.—We started our experiments on 39 strains of *Escherichia coli* with a concentration of 30 Oxford units of penicillin per

centimeter. The 16 resistant strains were tested with 45 or 60 Oxford units per cubic centimeter, and only 1 strain yielded to the action of penicillin at the latter concentration.

5. *Ps. Aeruginosa*.—As is shown in table 10, all the 3 strains of *Ps. aeruginosa* grew to innumerable after twenty-four hours' incubation in

urine containing 60 Oxford units of penicillin per cubic centimeter.

6. *Staph. Aureus*.—The extreme susceptibility of *Staph. aureus* to the action of penicillin has been universally established. We included this organism in our studies not only because it is

which was later found to be one of the most susceptible to the action of penicillin, gave no growth also at 2 and at 1 unit per cubic centimeter before incubation. This apparent anomaly was later explained by the fact that although these initial counts were labeled "in-

TABLE 9.—The Effect of Various Concentrations of Penicillin in Urine on 18 Strains of *Aerobacter Aerogenes*.

Strain	Number of Bacteria in 0.5 Cc. of Urine							
	60 Oxford Units per Cc.		45 Oxford Units per Cc.		30 Oxford Units per Cc.		15 Oxford Units per Cc.	
	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation
2	—	—	—	—	2,220	0	3,000	Innumerable
3	1,800	100	2,400	Innumerable	2,400	Innumerable	—	—
5	3,120	Innumerable	4,200	Innumerable	1,920	Innumerable	—	—
6	4,200	Innumerable	3,000	Innumerable	2,640	Innumerable	—	—
7	4,800	Innumerable	7,200	Innumerable	4,320	Innumerable	—	—
9	5,400	Innumerable	4,200	Innumerable	2,640	Innumerable	—	—
11	4,200	Innumerable	3,600	Innumerable	1,440	Innumerable	—	—
13	6,360	Innumerable	3,000	Innumerable	4,280	Innumerable	—	—
14	4,440	Innumerable	2,400	Innumerable	3,000	Innumerable	—	—
15	3,780	Innumerable	2,400	Innumerable	6,000	Innumerable	—	—
16	6,420	Innumerable	Innumerable	Innumerable	2,760	Innumerable	—	—
17	3,900	Innumerable	3,600	Innumerable	720	Innumerable	—	—
19	6,600	Innumerable	5,640	Innumerable	4,680	Innumerable	—	—
20	3,600	Innumerable	2,460	Innumerable	4,920	Innumerable	—	—
23	4,200	Innumerable	3,360	Innumerable	3,180	Innumerable	—	—
24	—	—	—	—	5,400	1	2,280	Innumerable
25	4,620	Innumerable	1,620	Innumerable	2,340	Innumerable	—	—
26	5,580	Innumerable	4,800	Innumerable	6,120	Innumerable	—	—

often encountered in urinary infections but also as a control for the other organisms on which we were trying out the effect of penicillin. During our work with this organism a few interesting facts were brought out.

TABLE 10.—The Effect of Penicillin on 3 Strains of *Pseudomonas Aeruginosa* in Urine Containing 60 Oxford Units per Cubic Centimeter

Strain	Number of Bacteria in 0.5 Cc. of Urine	
	Immediately After Inoculation	After 24 Hours' Incubation
1.....	6,540	Innumerable
2.....	11,320	Innumerable
3.....	8,220	Innumerable

TABLE 11.—The Effect of Relatively High Concentrations of Penicillin in Urine on 5 Strains of *Staphylococcus Aureus*

Strain	Number of Bacteria in 0.5 Cc. of Urine					
	4 Oxford Units per Cc.		2 Oxford Units per Cc.		1 Oxford Unit per Cc.	
	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation
1	0	0	0	0	0	0
3	2,100	5	4,260	4	5,430	240
6	0	0	1	0	120	0
8	0	0	2	0	35	21
9	0	0	3	0	2	0

Table 11 shows the results of one of our earlier experiments. With 4 Oxford units of penicillin per cubic centimeter of urine the initial plates "immediately after inoculation" of 4 of the 5 strains did not show any growth. Strain 1,

immediately after inoculation," some lapse of time was almost unavoidable between the inoculation of the organisms into the urine containing penicillin and the moment when the appropriate amount of inoculated urine had been transferred into the Petri dish and the sample was ready for plating with warm agar. Another point to be noted is that when 0.5 cc. of inoculated urin

TABLE 12.—The Effect of Penicillin on *Staphylococcus Aureus* in Urine in Relation to the Time of Incubation and Also the Amount of Urine Pour-Plated

Strain	Time of Incubation, Hours				
	0	½	2	6	24
	Number of Bacteria in 0.1 Cc. of Urine				
1	13	1	0	0	0
2	600	156	0	0	0
4	840	600	0	2	0
5	120	4	7	0	0
5	Number of Bacteria in 0.5 Cc. of Urine				
	0	0	0	0	0

was used for the plating with 10 cc. of warm agar, the resultant concentration of penicillin therein still retained strength sufficient to exert bactericidal action on the staphylococci suspended in the medium.

With 0.1 cc. of inoculated urine containing 4 Oxford units of penicillin per cubic centimeter the counts dropped tremendously with strains 2 and 5, from 13 and 126 to 1 and 4 respectively in half an hour's time (table 12). When 0.5 cc of inoculated urine with the same concentration of penicillin was used, strain 5 showed no growth

all, even when the "time of incubation" of the inoculated urine in the test tube was cut down to "O hour." Obviously, these organisms were gradually killed off while being suspended individually in the solid agar medium, which contained a sufficient concentration of penicillin to have a bactericidal effect even after dilution with the agar during incubation for twenty-four hours.

Table 13 shows that at a concentration as low as 0.033 Oxford unit of penicillin per cubic centimeter all of the 11 strains exhibited inhibition of growth. At 0.025 unit per cubic centimeter only strain 6 showed inhibition.

COMMENT

One outstanding fact that has perplexed both clinicians and laboratory workers is that penicillin is rapidly excreted through the kidneys

ment of certain types of infections of the urinary passages.

Our experiments have shown that 3 Oxford units of penicillin per cubic centimeter of urine is sufficient to reduce the number of inoculated fecal streptococci greatly after twenty-four hours' incubation. Urine from patients may contain as much penicillin as 120 Oxford units per cubic centimeter.⁸ Therefore it is likely that unless the kidney is too badly damaged the desired concentration of penicillin in urine can be readily attained, with a resultant curative effect on *Str. faecalis* infection of the urinary passages.

The results of our studies on *P. ammoniae* show that it is at least 4 times as susceptible to penicillin as *Esch. coli* but 240 times as resistant as *Staph. aureus*. This is in good agreement with the figures given by Florey and his co-workers, who found that *P. ammoniae* is

TABLE 13.—The Effect of Relatively Low Concentrations of Penicillin in Urine on 11 Strains of *Staphylococcus Aureus*

Strain	Number of Bacteria in 0.5 Cc. of Urine											
	½ Oxford Unit per Cc.		¼ Oxford Unit per Cc.		1/10 Oxford Unit per Cc.		1/20 Oxford Unit per Cc.		1/30 Oxford Unit per Cc.		1/40 Oxford Unit per Cc.	
	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation	Immediately After Inoculation	After 24 Hours' Incubation
1.....	224	1	5,880	3	2,700	85	780	1	2,340	240	1,380	Innumerable
2.....	2,100	6	2,400	60	2,640	35	5,460	8	5,940	660	2,880	Innumerable
3.....	3,300	600	1,380	478	2,160	1,320	1,980	600	1,680	600	2,040	Innumerable
4.....	1,500	6	1,560	2	2,040	29	2,160	7	2,100	56	2,280	Innumerable
5.....	2,820	34	1,200	0	1,920	184	2,820	480	2,400	360	3,180	Innumerable
6.....	480	49	2,040	16	Innumerable	1,220	1,200	4	4,080	85	2,520	600
7.....	1,200	23	1,920	11	1,920	13	1,200	2	4,080	91	6,540	Innumerable
8.....	4,800	74	11,880	104	3,900	16	2,200	300	2,200	155	4,200	Innumerable
9.....	1,980	15	1,860	2	1,380	15	2,060	2	3,900	420	3,980	Innumerable
10.....	2,040	41	1,260	13	2,940	45	2,160	0	3,900	420	2,580	Innumerable
11.....	680	9	1,620	0	540	5	1,500	5	1,500	77	1,080	Innumerable

in the urine. It appears in much higher concentrations in urine than in any other body fluids: Its concentration in the blood never approaches that found in the urine. With a normal renal function an output in the urine of 58 per cent⁷ of the 40,000 to 100,000 units of injected penicillin a day should give a concentration of from 20 to 60 units per cubic centimeter in the urine. In view of these high concentrations attainable in the urine, it would seem logical to infer that penicillin would be an ideal urinary antiseptic. The present communication, which is limited to in vitro studies covering the common bacterial flora encountered in infections of the urinary tract, distinctly shows such a potentiality. As the supply of penicillin has been steadily increasing, the time will soon arrive when penicillin will be available in quantity, and it may well play an important role in the treat-

ment of certain types of infections of the urinary passages. The low level of 8 Oxford units per cubic centimeter of urine at which *P. ammoniae* is reduced in number brings urinary infections with this bacillus into the range of successful treatment.

The work on *Esch. coli*, *A. aerogenes* and *Ps. aeruginosa* shows them to be of such a degree of resistance that penicillin may be of questionable value in clinical control of infections due to them. The sharp line of demarcation of *Esch. coli* into resistant and susceptible strains at 30 units per cubic centimeter, with little change at higher concentrations, is of interest and may well be of significance in clinical applications of these results.

The relative susceptibility of the various organisms studied is summarized in table 14. One thirtieth Oxford unit of penicillin per cubic centimeter of urine was sufficient to show definite

7. Rammelkamp, C. H., and Keefer, C. S.: The Absorption, Excretion, and Distribution of Penicillin, *Clin. Investigation* 22:425-437 (May) 1943.

8. Heilman, D. H.: Personal communication to the authors.

inhibition in all strains of *Staph. aureus*. *Str. faecalis* was 90 times as resistant as *Staph. aureus*, *P. ammoniae* 240 times as resistant, *Esch. coli* at least 900 times as resistant and *A. aerogenes* and *Ps. aeruginosa* at least 1,800

TABLE 14.—*The Relative Susceptibility of Various Organisms to Penicillin in Urine as Compared with That of Staphylococcus Aureus*

Bacteria	Oxford Units of Penicillin per Cc. of Urine Sufficient to Produce Inhibition	Susceptibility of Each Organism Relative to That of <i>Staphylococcus Aureus</i>
<i>Staphylococcus aureus</i>	1/30	1 : 1
<i>Streptococcus faecalis</i>	3	1 : 90
<i>Proteus ammoniae</i>	8	1 : 240
<i>Escherichia coli</i>	30 or more	1 : 900 or more
<i>Aerobacter aerogenes</i>	More than 60	1 : more than 1,800
<i>Pseudomonas aeruginosa</i> .	More than 60	1 : more than 1,800

times as resistant. These results agree fairly well with the observations of Florey and his co-workers and of others.

SUMMARY AND CONCLUSIONS

A detailed study of the bactericidal action of penicillin in urine on bacterial flora commonly encountered in urinary infections is presented. Thirty strains of *Streptococcus faecalis*, 39 strains of *Escherichia coli*, 13 strains of *Proteus ammoniae*, 18 strains of *Aerobacter aerogenes*, 3 strains of *Pseudomonas aeruginosa* and 11 strains of *Staphylococcus aureus*, all originally isolated from the urine of patients with various

infections of the urinary passages, were employed in these experiments. The following conclusions are drawn:

1. For *Str. faecalis* a concentration of 3 Oxford units of penicillin per cubic centimeter of urine is bactericidal.

2. For *Pr. ammoniae* 8 units per cubic centimeter of urine is the minimal bactericidal concentration of penicillin.

3. For *Esch. coli* there seems to be a demarcation between the resistant and susceptible strains at a level of 30 Oxford units of penicillin per cubic centimeter of urine.

4. *A. aerogenes* and *Ps. aeruginosa* are very resistant to the action of penicillin.

5. *Staph. aureus* has served satisfactorily in this investigation as a control for the other organisms under study as to their respective resistance and susceptibility toward the action of penicillin. The growth of this organism is inhibited at a concentration of 0.033 Oxford unit of penicillin per cubic centimeter of urine.

6. The bactericidal action of penicillin at a low level of its concentration in urine presents therapeutic possibilities for the treatment of urinary infections due to *Staph. aureus*, *Str. faecalis*, *P. ammoniae*. The resistance of *Esch. coli*, *aerogenes* and *Ps. aeruginosa* to penicillin practically rules it out as a means of treating these infections.

The Mayo Clinic.

ROENTGENOGRAPHIC APPEARANCE OF THE ESOPHAGUS IN NORMAL INFANTS

HARRY BAKWIN, M.D., AND ELEANOR GALENSON, M.D.

NEW YORK

AND BERNARD E. LEVINE, M.D.

BOSTON

Data on the roentgenographic appearance of the esophagus in infancy are meager. The only extensive study is that of Henderson¹ on the newborn. He found that the esophagus at this age appears as a straight or fusiform tube with smooth contours. The lower half nearly always extends to a greater size than the upper, and there may be considerable stasis in this portion.

METHOD OF STUDY

This series consisted of 32 infants, ranging in age from weeks to 22 months, chosen at random from the wards of Bellevue Hospital. All infants were well at the time of examination and were free from gastrointestinal symptoms. Several had recovered from minor infections.

The regular feeding was omitted, and in its place a mixture of barium sulfate and acacia, sweetened with sugar, was given.² The mixture was made thick enough to drip through a 2 mm. nipple opening at the rate of about 1 drop per second. Approximately two parts of barium sulfate and one part of powdered acacia mixed with warm water were used. Accurate proportions cannot be given, since the viscosity of the mixture varied with a number of factors, such as temperature, the order in which the component parts were added and the quality of the barium compound and of the acacia. The roentgenograms of all but 4 patients were taken with the infants in the supine position. Two ounces (50 cc.) of the mixture was offered. The exposure was made as soon as possible after the first few swallows. Films were taken simultaneously with the swallowing reflex. This was not always easy to judge, but three criteria were found helpful: tensing of the muscles of the neck, momentary cessation of respiration and slight contraction of the abdominal muscles.

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From the Children's Medical Service and the Department of Roentgenology, Bellevue Hospital, and the Department of Pediatrics, New York University.

1. Henderson, S. G.: The Gastrointestinal Tract in the Healthy Newborn Infant, *Am. J. Roentgenol.* **48**: 12, 1942.

2. Buckstein, J.: Clinical Roentgenology of the Alimentary Tract, Philadelphia, W. B. Saunders Company, 1940.

Roentgenograms were taken at a distance of 4 feet (1.2 meters). Though the distance between patient and tube was shorter than that ordinarily used with adults (2 meters), it is not likely that there was any significant distortion, since the depth of the chest in an infant is so much less than that in an adult. The time of exposure was one twentieth of a second and the milliamperage 200, with the voltage adjusted to the thickness of the chest. A fast Potter-Bucky diaphragm was used.

FLUOROSCOPIC OBSERVATIONS

As the infant swallowed the opaque mixture a narrow column could be seen descending rapidly through the esophagus (fig. 1 *A, B*). Ordinarily the material entered the stomach promptly at first, but as the feeding continued the cardiac orifice opened and closed intermittently (fig. 1 *C, D*). At times material accumulated in the esophagus, especially in its lower portion, which became considerably distended and bulbous (fig. 2 *A*). In some instances the esophagus contracted in its middle third as well as at the cardia, and in such instances the organ had the appearance of a dumbbell, with enlargements above and below the central portion (fig. 2 *B, C, D*). From time to time bubbles of gas could be seen in the esophagus. As these were regurgitated from the stomach the opaque mixture also passed back up from the stomach, and this might occur for a considerable length of time after the feeding was completed. The barium might rise the entire length of the esophagus and be expectorated, or it might pool in the lower portion, which then became distended (fig. 3 *B*).

ROENTGENOGRAMS

The contours were uniformly smooth. In general the esophagus was sinuously curved, with the convexity to the left above and to the right below, but this was not always the case. In some instances it was curved as though it were too long for the thorax (fig. 4).

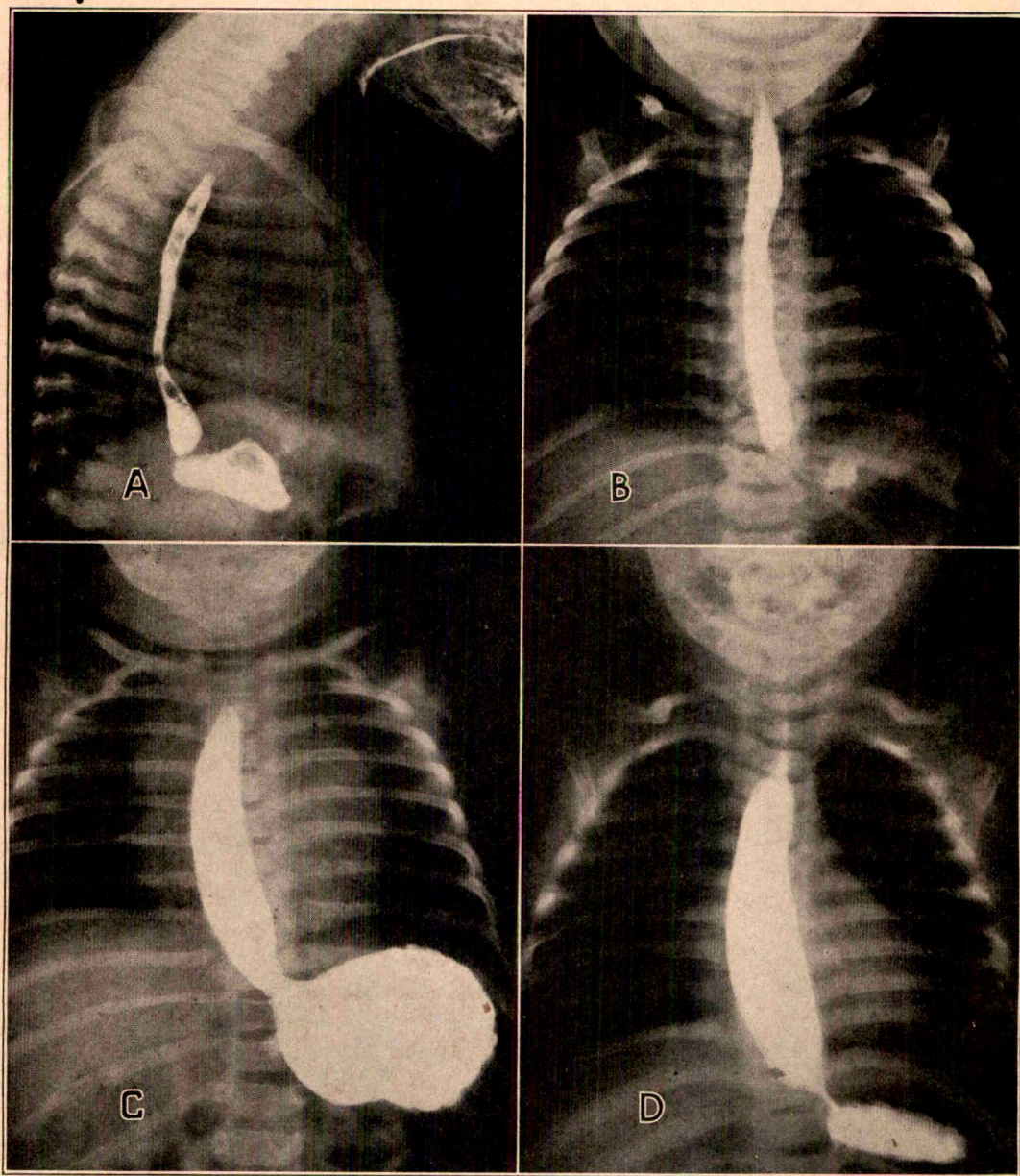


Fig. 1.—Esophagrams of normal infants. *A*. Five weeks old. The barium is mixed with air. The lower end of the esophagus shows normal expansion. *B*. Four months old. *C*. Seven weeks old. The subdiaphragmatic segment is wide. The maximum diameter of the esophagus is 14 mm. *D*. Two months old. The subdiaphragmatic segment is narrow. The maximum diameter of the esophagus is 19 mm.

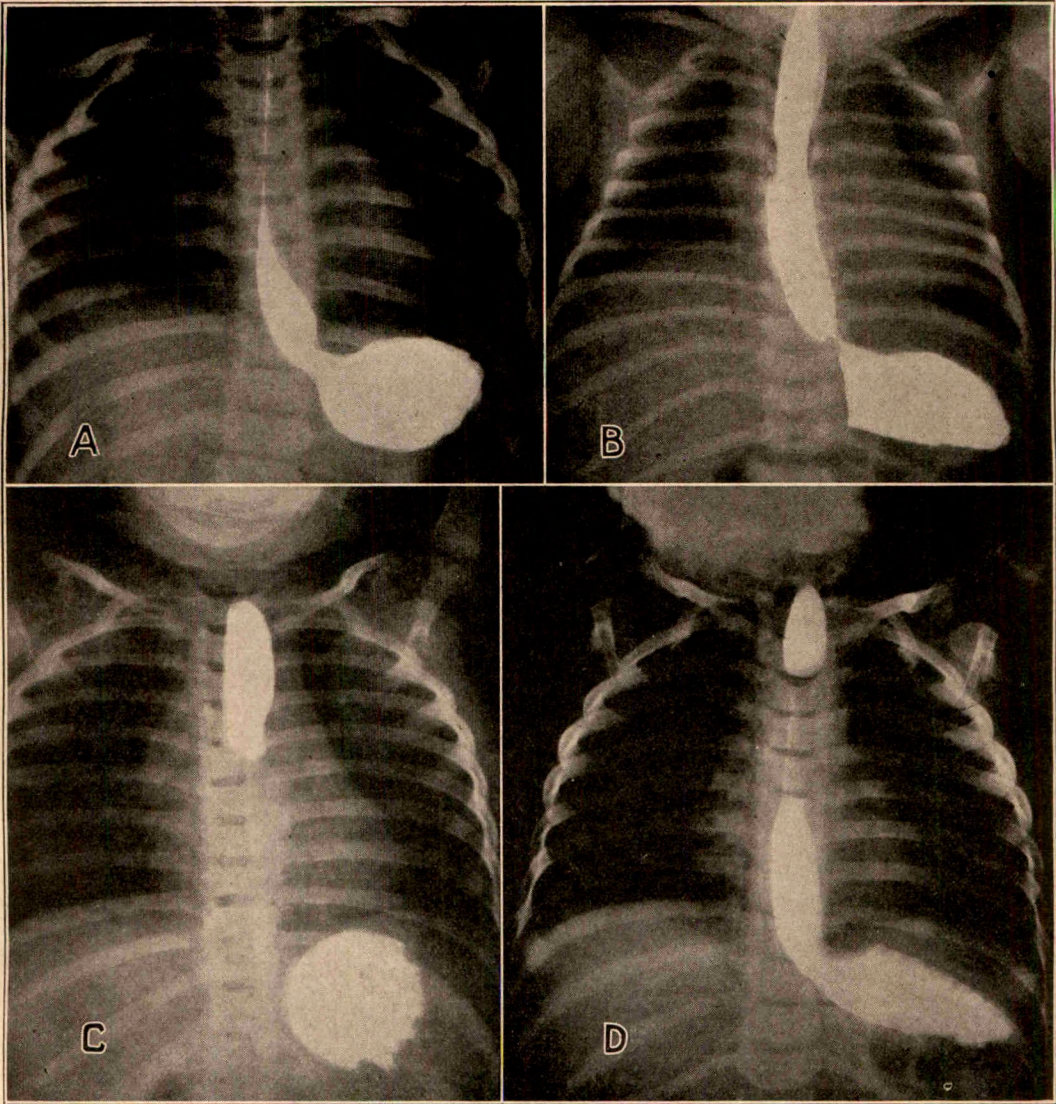


Fig. 2.—Esophagrams of normal infants. *A*. Twenty-two months of age. There is an accumulation of barium mixture in the lower third of the esophagus. *B*. Three weeks of age. The midportion shows a shallow constriction. *C*. Eighteen months of age. The barium mixture is momentarily retained in the upper third of the esophagus. *D*. Eighteen months of age. The upper and lower portions of the esophagus are filled with barium mixture; the middle portion is empty.

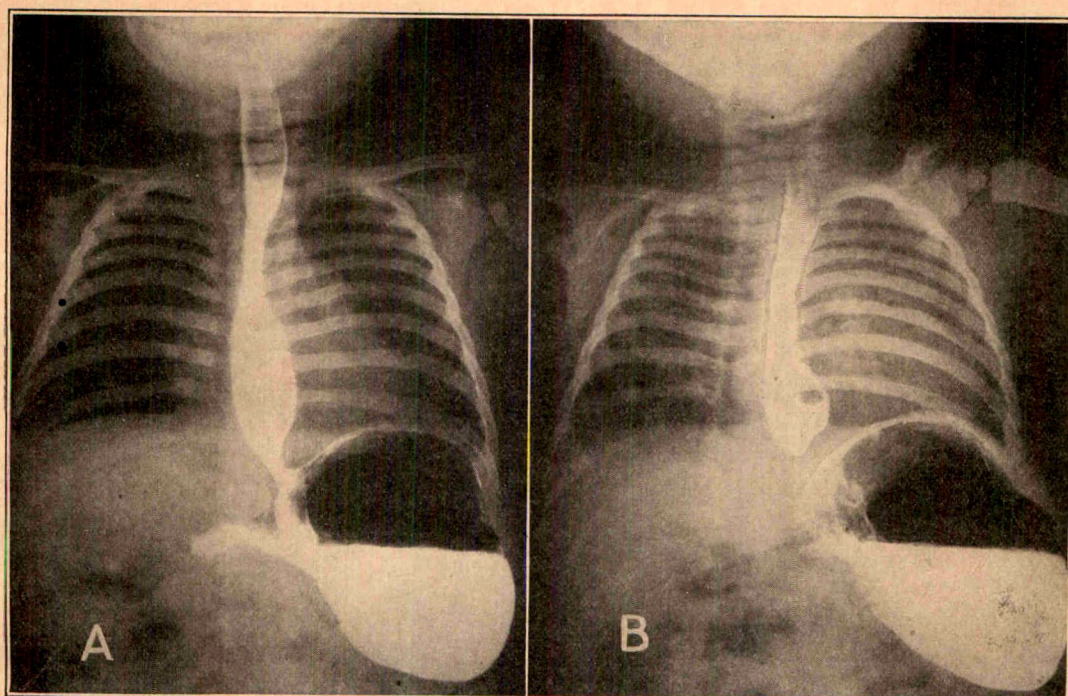


Fig. 3.—Esophagograms of an infant 6 months of age, showing the difference in configuration during the same feeding. *A* reveals the upper and lower thirds distended with barium mixture and air and the central third narrow. *B* shows pooling of the barium mixture in the lower segment of the esophagus (diameter of the bulbous portion, 16 mm.).

The esophagus in infants is markedly distensible. Roentgenograms taken during the course of a feeding of the barium-acacia mixture often showed an esophagus which was as wide as or wider than the vertebral column and which ap-

proximated in diameter that of a normal adult. In most instances the organ was narrow at the beginning of the feeding, with a diameter of about 4 to 8 mm., but it might be wide and distended with bubbles of gas from the start.

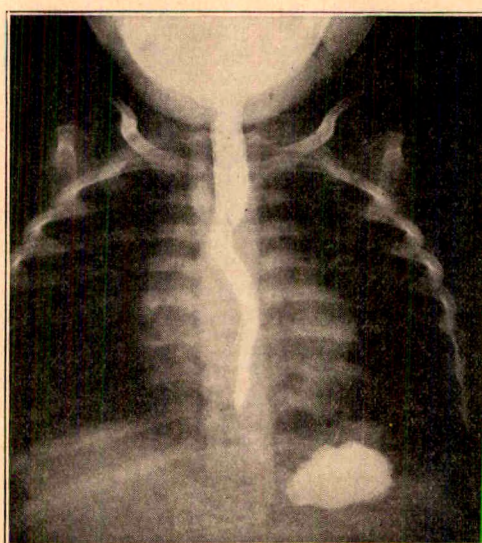


Fig. 4.—Esophagogram of a normal infant 16 months of age. The esophagus is tortuous.

The variability in the size and form of the esophagus in different infants is illustrated in figures 3 and 5. The films in figure 3, of an infant 6 months old, were taken during the meal feeding at an interval of a few minutes. The films in figure 5, of another infant, were taken on consecutive days. The diameter of the central portion of the esophagus in the film taken on Dec. 2, 1941 was 12 mm., and on the following day the diameter was 6 mm.

An accumulation of the barium mixture was occasionally seen ballooning out the lower portion of the esophagus several minutes after the feeding had been completed (fig. 3*B*). That this material was regurgitated from the stomach

for some time after a feeding has been completed may be falsely interpreted as due to retention, especially if the subdiaphragmatic portion of the esophagus is visualized as a narrow, thread-like channel. It is therefore important to keep in mind that the esophagus in an infant is distensible to a marked degree and that pooling of material in the lower portion for a considerable length of time after feeding is common and is ordinarily due to reflux from the stomach.

SUMMARY

Roentgen studies of the esophagus with an opaque meal were made on 32 normal infants ranging in age from 3 weeks to 22 months.

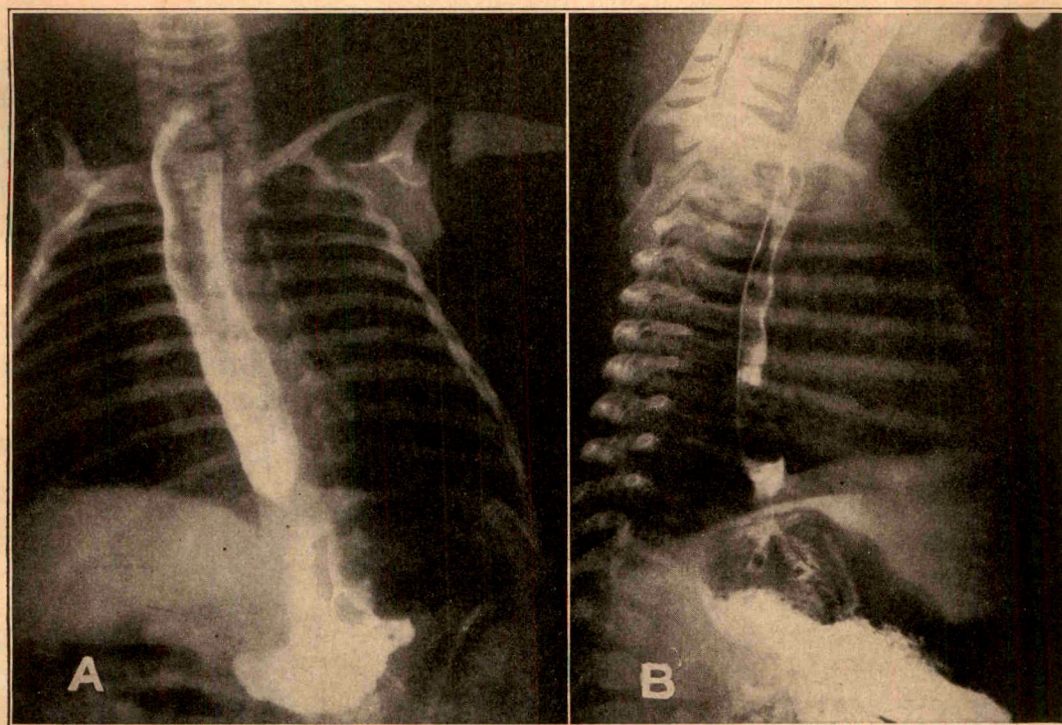


Fig. 5.—Esophagrams of a normal infant 2 months old, taken on consecutive days, illustrating the distensibility of the esophagus. *A*, film taken Dec. 2, 1941. *B*, film taken Dec. 3, 1941.

rather than retained in the esophagus by the contracted cardia was suggested by Dr. John Caffey³ and is evident from the fluoroscopic examinations. The subdiaphragmatic segment of the esophagus could often be seen below the accumulated material as a narrow channel leading into the stomach.

COMMENT

The wide shadow cast by the esophagus of an infant in a roentgen film may readily lead to an erroneous diagnosis of cardiospasm. Furthermore, the presence of food in the esophagus

The esophagus in the infant is a distensible tube and may be as wide as or wider than the vertebral column.

Accumulations of opaque material are commonly seen distending the lower portion of the esophagus during a meal. They may also be present for some time after a meal and are ordinarily due to regurgitation from the stomach rather than to stasis or obstruction at the cardia.

Dr. Jacob Buckstein gave valuable suggestions during this study.

132 East Seventy-First Street.
Bellevue Hospital.
636 Beacon Street.

3. Personal communication to the authors.

ROLE OF HEMOAGGLUTININS ANTI-A AND ANTI-B IN PATHOGENESIS OF JAUNDICE OF THE NEWBORN (ICTERUS NEONATORUM PRECOX)

I. HALBRECHT, M.D.

PETACH TIQUAH, PALESTINE

The work of Levine¹ and others on the importance of the Rh factor in the genesis of erythroblastosis fetalis has stimulated general interest in the problem of jaundice of the newborn. All authors now accept the view that all forms of icterus in the newborn, physiologic as well as pathologic, are hemolytic in origin and that the liver does not participate at all in their causation. The bile excretion function of the liver of the newborn has recently been examined by Eastman,² who found that bilirubin injected intravenously in 25 newborn infants with and without icterus was equally well excreted in all; thus he proved that the liver is not a factor in the genesis of icterus of the newborn.

The question of the cause of the hemolysis in the various forms of icterus of the newborn has been answered as far as erythroblastosis fetalis is concerned by Levine and others. In all probability the Rh factor is the cause of the destruction of blood which results in the various aspects of erythroblastosis fetalis, such as icterus gravis, congenital anemia of the newborn and the marked stimulation of the forming centers.

The question arises whether the same factor or a similar one, such as some other hemoagglutinin, can be held responsible for the production of other, milder varieties of icterus of the newborn and whether there is any connection between the physiologic and the pathologic forms of icterus of the newborn. It is interesting that, while different authors report widely different incidences of erythroblastosis fetalis, they report equal differences in mortality from this disease. Clifford and Hertig³ found erythroblastosis fetalis once in every 340 births, while Hellman⁴ found it only once in 1,500 births. It is obvious that the diagnosis of erythroblastosis fetalis is

far from being clearly differentiated; some authors have included conditions excluded by others. In the past several years I have investigated this problem, and the results are the subject of this paper.

PRESENTATION OF DATA

Among 10,000 births I found only 9 cases of true erythroblastosis fetalis with all the classic characteristics of the disease; there was a mortality of almost 60 per cent. I found 60 additional cases of a type of icterus which was similar in some respects to erythroblastosis fetalis, but which in other respects resembled physiologic icterus of the newborn. Like erythroblastosis fetalis, icterus in these cases appeared early—within twenty-four hours after birth—and was at times no less intense than that in erythroblastosis fetalis. As in children without jaundice or with the physiologic form, the prognosis in these cases was excellent. The children appeared well, nursed vigorously, were alert and showed no marked loss of weight. Hemorrhagic manifestations were lacking in all of them, and the liver and the spleen were not enlarged. I shall designate this early icterus as icterus precox, to differentiate it from icterus gravis and from physiologic icterus.

The blood of patients with icterus precox showed no changes from the normal. Of 11 children examined, only 3 showed a mild anemia and none had a larger number of nucleated red cells than is normal for this age. Quantitative indirect van der Bergh tests were done on the umbilical blood of a number of newborn infants. In 15 patients with icterus precox I found a marked increase of bilirubin, an average of 1.7 mg. per hundred cubic centimeters, with a minimum of 0.95 mg. and a maximum of 2.50 mg. In 13 newborn infants with physiologic icterus I found that the average level of bilirubin in the blood of the cord was 0.73 mg. per hundred cubic centimeters, the minimum 0.0 mg. and the maximum 1.10 mg., while for 60 newborn infants without icterus the figures were: average 0.55 mg., minimum 0.0 mg. and maximum 0.75 mg.

1. Levine, P., and others: Role of Isoimmunization in Pathogenesis of Erythroblastosis Fetalis, *Am. J. Obst. & Gynec.* **42**:925 (Dec.) 1941.

2. Linn, H., and Eastman, N. J.: Behavior of Intravenously Injected Bilirubin in Newborn Infants, *Am. J. Obst. & Gynec.* **33**:317, 1937.

3. Clifford, S. H., and Hertig, A.: Erythroblastosis of Newborn, *New England J. Med.* **207**:105, 1932.

4. Hellman, H., and Hertig, A.: Erythroblastosis, *Am. J. Obst. & Gynec.* **36**:137, 1938.

Of especial interest was the determination of the blood groups of the infants with icterus precox and of their mothers. Fifty-seven of the 60 infants, or 95 per cent, had blood incompatible with that of the mother, so that the serum of the latter agglutinated the red cells of the former. One hundred and sixty newborn children with physiologic icterus were examined during the same period, and only 48, or 30 per cent, had blood incompatible with that of the mother; while of 2,000 infants without icterus, only 530 (26.5 per cent) showed incompatibility (table 1).

TABLE 1.—*Compatibility of Blood of Children and of Mothers*

	Incompatible	Compatible	Total
Physiologic icterus.....	48	112	160
Icterus precox.....	57	3	60
Normal.....	530	1,470	2,000

COMMENT

The appearance of severe icterus several hours after birth has been noted by many obstetricians and pediatricians; the majority have classified this condition as physiologic icterus. Some authors, however, considered it a mild form of icterus gravis, and this explains the great differences in the incidence and the prognosis of icterus gravis reported by different observers.

I believe that this early benign icterus does not belong in the classification icterus gravis. Neither can it be included in the classification physiologic icterus, for I believe that in the genesis of icterus precox, or early benign icterus, a specific factor enters, the passage of isohemoagglutinins anti-A and anti-B from the mother to the child through the placenta. These agglutinins hemolyze the infant's red cells and produce an increase of bilirubin in the placental blood.

This is not a new concept. Lenart and Biro⁵ in 1927 already stated that hemoagglutinins are the cause of all icterus in the postnatal period. Their argument is not convincing, however, for they placed all forms of icterus in one group, produced by a single factor. I believe that the agglutinins anti-A and anti-B cause only icterus precox and not the usual physiologic icterus, which does not appear until twenty-four hours after birth.

The passage of these agglutinins from the mother to the fetus by way of the placenta has been demonstrated by Hirszfeld and Zborowski⁶

5. Lenart, G., and Biro, S.: Die Isoagglutination bei den Neugeborenen und ihre Beziehungen zum Icterus neonatorum, *Jahrb. f. Kinderh.* **124**:77, 1929.

6. Hirszfeld, L., and Zborowski, H.: Fundaments of Serologic Symbiosis Between Mother and Fetus, *Klin. Wchnschr.* **5**:741, 1926.

and others, who showed that in 30 per cent of newborn children it is possible to find hemoagglutinins, which disappear from the blood after a short time. It is obvious that they were not produced in the blood of the child but passed to the child from the mother through the placenta.

The agglutinins anti-A and anti-B are milder hemolytic agents for the newborn than the agglutinin anti-Rh, for the former are absorbed by the antigen secreted by the tissues, while the latter is absorbed only by the red blood cells, the Rh factor being present only in the erythrocytes and not in the tissues. It is possible that in infants of the nonsecretory type in regard to antigens A and B—a type which, according to Schiff, includes 20 per cent of all human beings—the anti-A and anti-B agglutinins may cause a condition more severe than icterus precox, perhaps even erythroblastosis fetalis (table 2).

TABLE 2.—*Data on Blood of 15 Infants with Icterus Precox*

No.	Blood Group		Bilirubin in Placental Blood, Mg.	Red Cells in Placental Blood, Millions	Nucleated Red Cells	Hemoglobin, Gm. per 100 Cc.	Sex
	Infant	Mother					
1	A	0	1.60	3.6	+	9.0	♂
2	A	0	1.50	5.7	—	17.0	♂
3	B	0	2.20	4.4	—	14.4	♂
4	A	0	1.85	4.5	—	18.6	♂
5	A	0	1.60	3.5	—	13.6	♂
6	A	0	1.75	5.5	800	17.4	♂
7	A	0	1.70	5.9	—	17.0	♂
8	A	0	1.85	5.5	—	17.0	♂
9	A	0	1.75	7.0	—	19.4	♂
10	B	0	2.50	—	—	—	♂
11	A	0	2.20	—	—	—	♂
12	A	0	1.30	—	—	—	♂
13	B	0	1.25	—	—	—	♂
14	A	0	1.30	4.5	2,000	15.2	♂
15	A	0	1.60	5.5	—	17.2	♂

SUMMARY

The special form of icterus that is described is characterized by its early appearance—within the first twenty-four hours after birth—and its intensity. In these two characteristics it resembles erythroblastosis fetalis; otherwise it is similar to the ordinary physiologic icterus.

In 95 per cent of the cases of icterus precox I found incompatibility of the blood groups of the mother and the child—three times as often as with physiologic icterus and four times as often as in newborn infants without icterus.

The bilirubin content of the placental blood in these newborn infants was on an average 1.75 mg. per hundred cubic centimeters, as against an average of 0.75 mg. in physiologic icterus and 0.55 mg. in children without icterus.

Beilinson Hospital.

BETTER HELP FOR SPEECH BEGINNINGS

EDNA HILL-YOUNG

DENVER

In this article on the beginnings of speech I am writing certain ideas and judgments which are the result of a lifetime of study and practical work in the field of children's speech. During the last twenty-one years I have aided in conducting a school for children with speech difficulties, called the Hill-Young School of Speech Correction. The school functioned for six years in Minneapolis and for thirteen years in Los Angeles; for two years it has been a part of the speech department of the University of Denver.

I am writing now to call the attention of the physicians who care for young children to the fact that during these years many parents have come to me with children whose speech was still undeveloped at the ages of from 5 to 10 years or older. These parents had been assured by their physicians that speech would come and that they should go home and not worry about any possible trouble. And what else can the doctors advise? Their work is not that of speech trainers. They get their cues from those who work with speech. If they were convinced of the reliability of a therapy which would bring more effective results than the present way of dealing with speech beginnings they would be glad to recommend it instead of saying, "Don't worry: Speech will come."

The work which I have done with speech was founded on an experience of my own in which between the ages of 15 and 22 years I changed all my movements of speech. My sounds were produced in a difficult way, and the movements were practically all different from those used by the average speaker. Between the ages of 15 and 22 I studied the movements of speech, constantly checking to find wherein my own movements were different from those of other persons. Gradually during this period I segregated the procedures which seemed to produce the elements of speech. From then on I worked with children, wherever I found them, who needed to be helped into better speech habits. This study slowly evolved what is now known as the "motokinesthetic method."

During these years I also searched for the beginnings of speech difficulties. I found the same kind of mistakes, such as "dis" for "this" and "thee" for "see," repeating themselves,

among children in the middle grades as well as in the kindergarten. I went outside the school group to study the speech of the young children in homes in the vicinity of the school. The same mistakes were found among them. I found young children between 2 and 3 repeating incorrect forms—growing daily more fixed in their use. I began to wonder whether this particular age group were not the one to concentrate on. I began to apply the motokinesthetic method carefully, one step at a time, giving the children feeling for the correct beginning, and found that they responded well to this kind of teaching. The greatest difference in the child of 2 and the child of 7 or 8 lies in the length of time necessary for the correct method of speaking to become habitual. Often a 2 year old would respond in two weeks to the use of the new form and very soon accept it as a part of his habits. The 7 year old could often be helped by the same method to say a word correctly the first time he was worked with, but the habit of the past was too strong to give up, and in everyday speech I heard the former habits continually repeating themselves for months. During the past twenty years I have regularly spent some time developing and building up the speech of young children from 1 to 3 years. I believe the results of my work justify urging all who are interested in developing normal speech to consider a change in the present methods of dealing with speech beginnings in young children.

There are ways of managing the behavior and environment which will tend to help the beginnings of normal speech. There are certain ways which encourage and aid the child; there are others which discourage him. In the first place a normal adjustment of father and mother is important. If parents have found the way to work out their own problems the child feels a sense of security and relies on a strength outside his own. All children need this. The emotional life developed under these conditions tends toward a normal general development as well as toward normal speech. If the father and mother are not well adjusted the child is likely to sense the emotional upset in the home and is often torn by conflicting emotions, though he is not aware whence they come. In such cases

here may be too much crying or laughing, various abnormal uses of the larger muscles, such as moving the arms up and down to show joy, and running abnormally fast. Usually there are tantrums as well. Such an emotional state is not conducive to learning to talk. If the period between 18 and 24 months of age goes by without the beginnings of speech, a child may continue his infantile means of expression until he has become habituated to their use, in which case the learning of speech is deferred. As the months pass, the child tends to gain speech less and less easily. The habits first used for expression tend to become more and more fixed and may be a serious handicap in the effort toward speech. It is important, then, that speech beginnings precede the formation of habits of expression which later may interfere with the normal gaining of the use of spoken language.

One of the mistakes commonly made is talking about the progress of little children in their presence. In the work at the Hill-Young School mothers have brought their speechless children to my associates and me and have commented in their presence, "William will not talk. When we ask him to say words he always refuses." Many a child is sensitive to the thought that is being expressed by the adult even though he cannot understand all the words. He is affected by worried looks in parental eyes and worried tones in the voices that are discussing him. He may feel that the discussion is centered on him, and this fact may cause him to respond even more negatively. One should not discuss the child in his presence.

Aside from all consideration of the psychological aspects of this subject, however, adults must keep in mind that definite muscular processes must be learned step by step before the child can talk easily. It is through this learned muscular coordination that all thought is to be expressed in the months and years lying ahead. A large percentage of children learn some of these speech processes incorrectly at first, in a trial and error fashion. Correction necessitates breaking up of these faultily learned sequences and substitution of correctly formed processes or patterns, which may involve simple movement, coordination of various movements or movement of an entirely different set of muscles from those which the child first learned to use. The new patterns may also involve changes in tension, pressure and timing.

Changes in any pattern tend to confuse muscular action. Conflicts between the first and second learning patterns frequently occur. The smoothness and fluency of the muscular movement necessary for good speech is interfered

with. A large percentage of young children stumble over their words for a period, until the learning becomes stabilized. A smaller percentage become so conditioned to the kind of speech used during this period of struggle that they do not complete the correction but retain a struggling form of speech which may help to lay a foundation for a life of stuttering.¹

The number of children who fail to acquire speech satisfactorily enough to have no after-effects in later years is large enough to make it imperative that one "do something about it" during the months when the best preventive measures are possible. And what are these preventive measures? They are based on a technic for training which makes learning speech a simpler task for the child who might otherwise get discouraged in his attempt to move on into speech. This technic has been built on the principle that when muscular learning is involved it is best to learn correctly when first learning; hence the advantage in the use of the motokinesthetic method when the child is not yet starting speech at the age of 18 to 24 months. It is safer to "do something about it" at this time than to wait until the age of 3 or 4 is reached, because progress is slower and more difficult at the later age.

The usual worried attitude, "Our child is not beginning to talk, and we wonder whether something is wrong with him," must be replaced by *this* attitude: "Our child is not yet talking at 2 years of age. This in itself is nothing to worry about, but since there are helps which can be given through training to combat any possible further delay and hasten the coming on of speech, we plan to give our child that help now." A careful study of the whole situation should be made, psychological and environmental factors being considered. In addition to possible adjustments of these factors, use should be made of the helps obtainable from the application of the motokinesthetic method, a technic which moves the mouth and stimulates the correct beginnings of definite words and later on of entire words. This method should be employed whenever the casual naming of objects over a period of time has not been sufficient to start speech.

For instance, to teach "foot" the mother may move the child's lower lip upward against the upper teeth, blowing air herself in similar fashion to start the word "foot"; then she should immediately move the lower lip downward a little and toward the midline, sounding the vowel. The feeling of the production of the first two sounds in "foot" will stay within the muscles, and a

1. Hahn, E.: *Stuttering*, Stanford University, Calif., Stanford University Press, 1943, p. 49.

kinesthetic memory will thus be built up in association with the visual and auditory patterns. Several repetitions of the correct pattern tend to prevent the substitution of the "t" sound, in which the end of the tongue begins functioning instead of the lower lip, thus producing "toot." One should not expect immediate results from these "lessons." Beginnings should be stimulated, the word spoken casually and the child left to attempt the word when and where he wishes to do so. This technic stimulates the exact muscles which normally start the given word; the feeling of *how* to move, how much tension and pressure to apply and what timing is required—all is stimulated in one pattern.

The young child should never be forced into a lesson or into asking for things. There is a better, happier way. One too often takes it for granted that a young child *can* talk if he *will*, not understanding that a certain amount of learning and achievement precedes the automatic use of speech muscles.

The motokinesthetic stimulations which help the child toward the gaining of speech are many. They have been published elsewhere.² The present article can only be suggestive. If the technic has been mastered by the adults the training of the child to speak correctly, saying "come," not "tum," "see," not "tee," "I go," not "me do," and so on, is a delightful, profitable experience for the child and a happy one for the parents as well. Personality blossoms as the child finds in the beginning the correct way to express himself readily and easily. If correct learning is delayed too long the personality becomes dwarfed, restricted and emotionally warped. Fluent speech offers the greatest variety of opportunity for energy expenditure making for spontaneity and freedom and normal emotional outlet.

2. Stinchfield, S. M., and Young, E. H.: *Children with Delayed or Defective Speech*, Stanford University, Calif., Stanford University Press, 1938.

THE BONE MARROW AS AN ALTERNATE ROUTE FOR TRANSFUSION IN PEDIATRICS

HENRY A. REISMAN, M.D., AND IRVING A. TAINSKY, M.D.

JAMAICA, N. Y.

BROOKLYN

Henning¹ was the first to use the bone marrow as a route for transfusion. He tried to visualize the structure of the sternal bone marrow by the injection of watery contrast substances, such as abrodil (monoiodomethane sulfonic acid) and iopax (sodium salt of α -oxo- β -iodopyridine-N-acetic acid), and failed because of the comparative density of the sternum. On the other hand, postmortem experiments showed that the presence of contrast substances could be noted in both internal mammary veins after injection into the sternal bone marrow. When denser contrast substances, such as iodized sesame oil, were injected into the sternum, they were visualized roentgenologically. It was found that substances injected into the bone marrow entered the general circulation apparently unchanged and almost as rapidly as when injected intravenously. Tocantins and his associates² have shown that when mercury is injected into the bone marrow the metal may be seen by fluoroscopy to escape rapidly through the emissary veins into the general circulation.

The intramarrow method of infusion is useful when the veins of the extremities have all been damaged by repeated use or cannot be found, as in peripheral circulatory collapse, which prevents sufficient filling of the veins.³ It is indicated when intravenous administration is impossible because of widespread mutilation,

burns, edema, poorly developed or obliterated veins or shock.⁴ For patients suffering from acute peripheral collapse with cardiac decompensation and for persons under insulin shock, who must have large amounts of material injected into the general circulation directly and in whom intravenous injection is impossible because of lowered circulatory flow or collapse of the peripheral veins, the bone marrow route offers the best solution. In the newborn and in other infants the accessible veins are very poorly developed. The superior longitudinal sinus, the jugular veins or the scalp veins offer too great a risk, or extreme dexterity on the part of the operator is required; hence the intramedullary route offers a good substitute. By this means advantage can be taken of a rapid method of introduction of blood as well as other fluids into the circulation.

The sites of election vary with the size of the patient. Many of the workers at the present time suggest that in children under 3 years of age one should use the upper portion of the tibia or the lower portion of the femur.^{2b} The femur and the tibia are preferable to other sites in children because the density of the cortical layers of these bones is equivalent to that of the sternum or of the clavicle in adults. In patients above 2 years of age the site of election may be the manubrium of the sternum. It should always be kept in mind that the thinness and softness of the bony plates of the sternum in children do not allow as easy a differentiation to be made between the cortical layer and the marrow as is the case with adults. Though there are minor differences in the size of the marrow in infants and children, we prefer the following sites: the junction of the upper and the middle third of the tibia as first choice and as second choice the junction of the middle and the distal third of the femur. These sites are chosen because of their nearness to the surface of the body, the smallness of the amount of sub-

From the Department of Pediatrics of Queens General Hospital, Jamaica, N. Y.; Director, Dr. Henry A. Reisman.

1. Henning, N.: The Intrasternal Injection and Transfusion as Substitutes of the Intravenous Methods, *Deutsche med. Wchnschr.* **66**:737 (July 5) 1940.

2. (a) Jones, R. M.: A New Needle for the Treatment of Shock by Sternal Infusion, *Surg., Gynec. & Obst.* **76**:587 (May) 1943. (b) Tocantins, L. M.; Price, A. H., and O'Neill, J. F.: Infusions via Bone Marrow in Children, *Pennsylvania M. J.* **42**:1267 (Sept.) 1943.

3. (a) Tocantins, L. M., and O'Neill, J. F.: Infusion of Blood and Other Fluids into the Circulation via the Bone Marrow, *Proc. Soc. Exper. Biol. & Med.* **45**:782 (Dec.) 1940. (b) Tocantins, L. M.; O'Neill, J. F., and Price, A. H.: Infusions of Blood and Other Fluids via the Bone Marrow in Traumatic Shock and Other Forms of Peripheral Circulatory Failure, *Ann. Surg.* **114**:1085 (Dec.) 1941.

4. (a) Papper, E. M., and Rovenstine, E. A.: Utility of Marrow Cavity of Sternum for Parenteral Fluid Therapy, *War Med.* **2**:277 (March) 1942. (b) Tocantins and O'Neill.^{3a} (c) Tocantins, O'Neill and Price.^{3b}

cutaneous tissue present and the absence of intervening structures of any physiologic import, such as arteries, veins and nerves. It is not advisable to use the sternum in children under 2 years of age.^{2b} We prefer to use the tibia rather than the femur because a shorter needle will allow entrance into the marrow proper. The thick muscles and intervening tissue about the femur make it necessary to use a longer needle. This needle is likely to bend under the pressure required to penetrate the bone.

In order to avoid the possibility of injury to the epiphysal cartilage, it is advisable that the needle be directed toward the diaphysis. Once the flow has started the leg should be raised slightly above the level of the body.

The danger of fat emboli has been minimized by Harris, Perrett and MacLachlin.⁵

Blood given through the marrow enters the circulation almost as rapidly as by the intravenous route. According to Papper,⁶ the circulation time after sternal injection as determined by the macasol test is slightly, but not significantly, less than that after intravenous injection. His figures indicate that the material is absorbed from the sternal marrow at least as rapidly as from a vein. The cyanide test indicated that absorption from the sternum into the general circulation is more rapid than from a vein. The average end point after intravenous injection was fifteen and five-tenths seconds and after sternal injection only eleven and four-tenths seconds. Meyer and Perlmuter, using the intravenous and intramedullary route, found the circulation time to be essentially the same in 21 subjects. In 2 cases of cardiac decompensation the circulation time from marrow to tongue was less than the venous time. In a third case the results were identical.

The technic of intramarow infusions is not difficult to master. Henning preferred a needle without a stylet.¹ The more recent investigators prefer a needle with a stylet.⁷ In the case of femoral or tibial puncture the lateral surface is preferred. After preliminary preparation of the skin the needle is inserted vertically, with the

bevel up. The osteum is penetrated with rotary type of pressure until the compact layer is pierced and the needle enters the marrow. In the case of sternal puncture the puncture is made in the midline of the sternum at the level of the third, fourth or fifth intercostal space. A sensation similar to the cracking of an eggshell is usually heard or felt in the passage through the cortical layer into the marrow proper. On aspiration a pinkish fluid is withdrawn. This indicates that the needle is in the bone marrow.

Some workers feel that no aspiration of the marrow should be attempted.¹ The more recent opinion is that if a small syringe—one of 2 cc.—filled with isotonic solution of sodium chloride is used—gentle aspiration may be made. If on aspiration the saline solution in the syringe becomes pinkish and only slight pressure on the syringe barrel is necessary for emptying one may be reasonably sure the needle is in the marrow proper. Our feeling is that only by gentle aspiration and viewing the pinkish discoloration can we be reasonably confident that it is time to start the infusion. One will note that on manipulation there are definite directions of flow from the needle into the marrow which offer less resistance than others. The needle should be left in one of these positions.

The blood may be given either by syringe or by means of a reservoir and slow drip. The syringe is used when less than 100 cc. of fluid is to be given or when rapid instillation is essential; the reservoir method, if large amounts are being given or if a slow drip method is necessary.

Our practice has been to flush the needle through with 2 cc. of isotonic solution of sodium chloride and then with a syringe of the material to be infused, before the reservoir is connected to the bone marrow needle. This is done to guard against clotting in the bone marrow or needle. Tocantins and his associates⁸ have suggested that one may use two bone marrow needles inserted into the sternum in order to obtain a more rapid rate of flow. This procedure probably could be adapted to pediatric practice. Should the emergency be sufficiently grave one may insert one needle into the femur and another into the tibia and connect the two needles by rubber tubes and a Y tube.

We have used two types of B.-D. needles. The smaller is a no. 19 gage needle, and the length of the shaft is $\frac{1}{2}$ inch (1.3 cm.); the larger is a no. 18 gage needle, and the length

5. Harris, Perrett and MacLachlin, cited by Tocantins, L. M., and O'Neill, J. F.: Infusions of Blood and Other Fluids into the General Circulation via the Bone Marrow: Techniques and Results, *Surg., Gynec. & Obst.* **73**:231 (Sept.) 1941.

6. Papper, E. M.: The Bone Marrow Route for Injecting Fluids and Drugs into the General Circulation, *Anesthesiology* **3**:307 (May) 1942.

7. (a) Jones.^{2a} (b) Papper.⁶ (c) Papper and Rovenstine.^{4a} (d) Tocantins, L. M.; O'Neill, J. F., and Jones, H. W.: Infusions of Blood and Other Fluids via the Bone Marrow: Application in Pediatrics, *J. A. M. A.* **117**:1229 (Oct. 11) 1941.

8. O'Neill, J. F.; Tocantins, L. M., and Price, A. H.: Further Experiences with the Technique of Administering Blood and Other Fluids via the Bone Marrow, *North Carolina M. J.* **3**:495 (Sept.) 1942.

f the shaft is 1 inch (2.5 cm.). Because of the difficulty of obtaining at the present time either this type of needle or any other satisfactory bone marrow needle, we have found that a special B.-D. spinal tap needle cut down to the proper length is satisfactory. It has been our practice to use the 19 gage needle for children under 6 months of age and the 18 gage needle for older children. We do not recommend using any needle larger than an 18 gage, because of the possibility of chipping the bone, the speedy outflow from the needle and the danger of making too large a puncture.

Proper splinting of the child's hip, knee and ankle is imperative. An effective method of maintaining the foot in the proper position is the use of the so-called "clove hitch" about the ankle, with traction made to the foot of the bed at the end of the splint board.⁸ To avoid interference with venous return, no constricting clothing or bandage should be applied to the extremity above the site of puncture. Our method has been to apply only two strips of adhesive tape about 1 inch (2.54 cm.) wide to the limb. One strip is placed over the patella and secured under the splint board. The second is placed about the arch of the foot and around the ankle; the foot is rotated externally, and the end of the adhesive tape is fastened to the bottom of the splint board. This method is used satisfactorily for both tibial and femoral punctures.

Because of the tendency of bone marrow to coagulate, if there is any evidence of obstruction in the flow the needle should be manipulated and the stylet replaced to guard against possible clotting in the needle. Occasionally it may be necessary to inject some isotonic solution of sodium chloride to start the flow again. The rate of injection is usually much slower than that used for intravenous drip. Too rapid a rate of injection by the syringe method may cause edema in the surrounding tissues of the limb because of the backflow of venous blood through the emissary veins. It is well to remember that when large quantities of fluids are given over a long period the rate of flow may change. This condition can be corrected by raising or lowering the height of the reservoir. For the ordinary drip method the height of the reservoir should be kept above 1 meter. Reversal of the direction of flow should not be permitted.

When an infusion has been completed the needle should be grasped firmly with one hand and the patient's limb with the other. The needle is then removed by a simultaneous rotary and withdrawing motion similar to that used in inserting it. The site of the puncture should be covered with a small sterile dressing; with

an infant one should take the added precaution of sealing the entire dressing with adhesive tape for two days to prevent contamination from feces and urine.

This method should be employed only by persons experienced in the technic and should be used with considerable caution. Experience has shown that it is not advisable to inject material through the needle unless a bone marrow mixture has been obtained by aspiration.⁹ A reversal of the direction of flow may cause clogging of the needle and should be avoided. Just as in intravenous infusion, a rapid rate of injection is not advisable. We have consistently used and found satisfactory a drip rate of about 10 drops per minute. When sternal punctures are attempted one must guard against piercing the posterior plate and injecting material into the anterior mediastinum. It is well to remember that if one needle puncture is made into a bone and an adjacent site is used soon after, especially if great pressure is applied, a "blow-out" of the primary site may result. We use the term blowout to describe an ejection of the marrow clot through a puncture site with resulting passage from the marrow to and through the periosteum. We feel that intramedullary infusions are contraindicated in cases of generalized infections accompanied by bacteremia or septicemia and osteomyelitis.¹⁰ If the needle is left too long in situ infection may result. Hypertonic or other irritating solutions which may also be sclerosing in action should not be given by the intramarrow method. Difficulty may be encountered in entering the marrow, particularly in some cases of anemia that produces an abnormal degree of ossification of the bone. In such instances we have found tapping the needle gently with a small mallet helpful in getting it into the marrow.

In addition to the conventional isotonic and hypotonic solutions used, the following are generally used in bone marrow infusions: blood plasma, blood, 5 per cent dextrose in isotonic solution of sodium chloride and sodium pentothal. The last-mentioned drug is now being used extensively under war conditions in intramarrow anesthetization on the battlefields and offers much for civilian medicine. Anesthesia was produced as rapidly and as readily by the intramarrow as by the intravenous route. The practical application of this method of anes-

9. Jones.^{2a} O'Neill, Tocantins and Price.⁸ Papper.⁸ Papper and Rovenstine.^{4a} Tocantins and O'Neill.⁵ Tocantins, O'Neill and Jones.^{7d} Tocantins, O'Neill and Price.^{2b}

10. Tocantins, O'Neill and Jones.^{7d} Tocantins, Price and O'Neill.^{2b}

thetia in pediatric surgery should not be overlooked.

Complications of this procedure are similar to those encountered in intravenous infusions, for example, entering the surrounding tissues instead of the marrow or going through the bone and out of the posterior cortical layer. Routine preparations for blood transfusion using the bone marrow route, such as typing, are the same as for the intravenous route. Several cases have been reported in which the posterior plate of the sternum was pierced, with the fluid entering the anterior mediastinum and also of so-called "blowouts." The following case indicates one of the hazards of this procedure and the only untoward reaction we have had.

REPORT OF A CASE

A newborn white boy, weighing 4 pounds $3\frac{1}{4}$ ounces (1,907 Gm.) at birth, which was premature, showed symptoms of erythroblastosis fetalis. The patient was given 30 cc. of Rh-negative type O blood in the distal portion of the left femur; the following day he received

30 cc. of Rh-negative type O blood in the distal portion of the right femur and then a third transfusion in the left femur. The general condition of the patient appeared to improve. The following day a fairly hard palpable mass was noted over the distal portion of the left femur, with definite tenderness and ecchymosis. On July 23 roentgen examination showed considerable swelling in the soft tissue structures in the prepatella region, with no osseous pathologic changes in the femur, fibula or tibia. On July 29 the area on the medial proximal part of the left knee broke down, with a subsequent discharge of a large amount of greenish yellow pus. The condition remained unimproved by splinting and local therapy. On October 10 a roentgen examination revealed some periosteal thickening along the distal fourth of the femoral diaphysis with the articular surfaces normal and moderate prepatellar edema but no definite evidence of osteomyelitis. Local drainage and application of a 5 per cent aqueous solution of sodium sulfathiazole and of a 1:10,000 solution of zephiran chloride solution locally with continuous splinting of the leg in extension improved the condition. Fortunately, the infant continued to make good progress, and he was subsequently discharged.

8803 One Hundred and Forty-Sixth Street.
247 Ocean View Avenue.

RESERVES, ABSORPTION AND PLASMA LEVELS OF VITAMIN A IN PREMATURE INFANTS

THOMAS H. HENLEY, M.D.; MARGARET DANN, M.D.,
AND WALTER R. C. GOLDEN, Ph.D.

ITHACA, NEW YORK

The immaturity of organs and enzyme systems contributes greatly to the difficulty of neonatal adjustment of premature infants. Their special needs for minerals and vitamins have been discussed by Levine and Gordon.¹ The degree to which absorption, storage and requirement of vitamin A are influenced by prematurity is a subject on which there is little information.

Accurate methods for the determination of the vitamin A content of plasma are now available for clinical use, but because of the wide range of values found in normal persons the results are difficult to interpret. Lewis and his associates have shown a relation between plasma levels, intake and hepatic stores of vitamin A in animals.² This relationship has also been suggested for human infants,³ though it may be altered in the neonatal period because of immaturity of the mechanism for mobilization of the vitamin from body stores.⁴

The present investigation consists of three series of observations: (1) study of the rise of vitamin A in the plasma of 21 infants given standard dose of vitamin A and concomitant determination of the excretion of fat by 10 infants; (2) determination of the levels of vitamin A in the plasma of 89 premature infants at or about 3 weeks of age and their relation to birth weight and vitamin intake; (3) examination for carotene and vitamin A of the livers of 3 infants who died at or shortly after birth.

From the New York Hospital and the Departments of Pediatrics and Public Health, Cornell University Medical College.

1. Levine, S. Z., and Gordon, H. H.: Physiologic handicaps of the Premature Infant: I. Their pathogenesis, *Am. J. Dis. Child.* **64**:274 (Aug.) 1942.

2. Lewis, J. M.; Bodansky, O.; Falk, K. G., and McGuire, G.: Relationship of Vitamin A Blood Level in the Rat to Vitamin A Intake and to Liver Storage, *Proc. Soc. Exper. Biol. & Med.* **46**:248 (Feb.) 1941.

3. Lewis, J. M.; Bodansky, O., and Haig, C.: Level of Vitamin A in the Blood as an Index of Vitamin A deficiency in Infants and Children, *Am. J. Dis. Child.* **2**:1129 (Dec.) 1941.

4. Lewis, J. M.; Bodansky, O., and Shapiro, L. M.: Regulation of Level of Vitamin A in Blood of Newborn Infants, *Am. J. Dis. Child.* **66**:503 (Nov.) 1943.

SELECTION OF SUBJECTS

Absorption of Vitamin A.—Tests were made on 20 thriving premature and full term infants from 6 to 70 days of age.⁵ The premature infants weighed less than 2,500 Gm. at birth, but at the time of the tests some had exceeded this weight. The full term infants weighed more than 2,500 Gm. at birth; some had not regained their birth weight at the time of the test. All infants were free from infection, jaundice and gastrointestinal disease. Except for 1 infant fed on human milk all received a standard formula of evaporated milk, dextrimaltose or cane sugar and water, with no vitamin A supplement for twenty-four hours.

A modification of the vitamin A absorption test described by May, Blackfan, McCreary and Allen⁶ was used. An oral test dose of 0.22 cc. of percomorph liver oil⁷ per kilogram (0.1 cc. per pound) of body weight was given, and blood plasma levels were determined before and five hours after ingestion. A rise of 29 units or more above the fasting level was arbitrarily chosen to indicate good absorption of vitamin A.

Excretion of Fat.—Analyses for total fat in feces collected for seventy-two hour periods were made for 8 premature and 2 full term infants⁸ during or immediately preceding the vitamin A absorption tests. The infants were all fed the aforementioned standard formulas containing an average of 120 calories per kilogram. The actual consumption of formula was calculated as 95 per cent of the formula as prepared, an average of 5 per cent of the intake being lost by adherence to bottles and nipples and by regurgitation, as

5. Dr. H. J. Stander, head of the department of obstetrics, gave us permission to study the full term infants.

6. May, C. D.; Blackfan, K. D.; McCreary, J. F., and Allen, F. H., Jr.: Clinical Studies of Vitamin A in Infants and in Children, *Am. J. Dis. Child.* **59**:1167 (June) 1940.

7. 60,000 U. S. P. units of vitamin A per gram (0.9 cc.) (Mead Johnson and Company preparation).

8. One full term infant was malnourished and was therefore not included.

determined by Gordon, Levine, Deamer and McNamara.⁹ Previous studies in this laboratory have shown the fat content of evaporated milk to average 8 per cent.

In accordance with the results of Gordon and McNamara,¹⁰ an arbitrary dividing line of 60 per cent of the dry weight of the feces excreted as fat was used to separate the infants with excessive loss of fat from those with normal excretion.

Levels of Vitamin A in the Plasma of Premature Infants.—Determinations of vitamin A in the plasma were made on or about the third week of life for a series of 89 premature infants.¹¹ The vitamin A intake, maintained for each baby at a constant daily level from the third day of life until the day preceding the test, varied for the different infants from 60 to 24,000 U. S. P. units daily (table 1). Vitamin A assays of

milk and milk products were performed in this laboratory.

The birth weights of the infants ranged from 1,176 to 2,506 Gm.; 8 babies weighed less than 1,500 Gm. at birth, 11 between 1,500 and 1,699, 16 between 1,700 and 1,899, 21 between 1,900 and 2,099, 22 between 2,100 and 2,299 and 11 above 2,300. Only 3 of the infants were Negro. There were 39 male and 50 female patients. The series included 7 pairs of twins.

Babies admitted to the premature infants' unit between November 1941 and April 1943 who remained in good condition were included in this part of the study. Approximately 30 per cent of the original group were later dropped from the series, primarily because they were discharged from the hospital before the eighteenth day of life. A few were excluded because of diarrhea.

TABLE 1.—Intake of Vitamin A and Carotenoids by Premature Infants

Milk Ingredient of Formula	Per 100 Gm. or Cc. of Milk					Daily Intake		
	Carotenoids		Vitamin A		Total Vitamin A Value, U. S. P. Units	Per Kg. of Body Weight		Per Infant, [†] Vitamin A U. S. P. Units
	Micro- grams	Vitamin A Equivalent,* U. S. P. Units	Micro- grams	U. S. P. Units *		Gm. or Cc.	Vitamin A U. S. P. Units	
Human milk.....	50	83	76	216.6	300	130-200	390-600	900
Evaporated whole cow's milk.....	75	124.5	37	162.5	287	55-70	158-190	350
Alacta.....	0	0	34	189.4	182	16-20	27-36	60
Supplement ‡						Vitamin A		
						U. S. P. Units per Gm.	U. S. P. Units per Infant §	
Synthetic oleovitamin D.....						0	0	
Special mixture.....						12,000	4,500	
Oleovitamin A and D.....						60,000	23,000	
Navitol-S.....						55,000	23,000	

* One microgram of carotenoids has a vitamin A value of 1.66 U. S. P. units. One microgram of vitamin A = 2.85 U. S. P. units.
† Average weight 2 Kg.
‡ Calculated from manufacturer's claims.
§ Dose 15 drops (approximately 0.375 Gm.).

9. Gordon, H. H.; Levine, S. Z.; Deamer, W. C., and McNamara, H.: Respiratory Metabolism in Infancy and in Childhood: XXIII. Daily Energy Requirements of Premature Infants, *Am. J. Dis. Child.* 59:1185 (June) 1940.

10. Gordon, H. H., and McNamara, H.: Fat Excretion of Premature Infants, *Am. J. Dis. Child.* 62: 328 (Aug.) 1941.

11. The analyses were made on the twenty-first day in 74 of the 89 cases. In the remaining 15 cases the day of the test was as follows:

Age, days	Number of Cases
14	1
18	2
19	2
20	3
22	5
23	2

(All but 4 infants were born in the New York Hospital.)

or a febrile illness or because of technical difficulties in obtaining or assaying the blood specimens. Nine babies who were discharged between 14 and 18 days of age and whose mothers were instructed to give a specified supplement daily except for the twenty-four hours prior to attending the outpatient department were included in the series.

The infants in this group of observations received three types of formulas: (1) whole, boiled human milk; (2) evaporated cow's milk, water and cane sugar; (3) Alacta,¹² water and cane sugar. Each formula was prescribed to furnish from 100 to 130 calories per kilogram of body weight per day.

12. Alacta is a preparation of cow's milk from which more than half of the fat has been removed.

The daily vitamin supplement consisted of 15 drops of one of the following preparations:

1. Synthetic oleovitamin D U. S. P. (vicsterol in oil).
2. A mixture of 4 parts of synthetic oleovitamin D U. S. P. with 1 part oleovitamin A and D (natural) U. S. P.
3. Oleovitamin A and D (natural) U. S. P.
4. Navitol-S.¹³

The vitamin A content of the diet and supplements is shown in table 1. Rotation of formulas and supplements in order of admission of the patients was later abandoned when it became evident that no correlation existed between the levels of vitamin A in the plasma and the type of formula ingested. From December 1941 through June 1942 supplements 1, 2 and 3 were prescribed approximately in rotation; from August 1942 through January 1943 supplements 1 and 4 were prescribed for alternate patients, and in February and March 1943 supplement 3 was given to all babies. The supplements were given by dropper separately from the formulas and were well tolerated in all instances.

Autopsy Material.—Samples of the livers of 23 premature and mature infants were obtained at autopsy.¹⁴ These infants, 16 premature and 7 mature, died within twenty-four hours after birth from causes not thought to have influenced the vitamin A content of the liver, the anatomic diagnosis being one or more of the following: prematurity, intracranial hemorrhage, atelectasis. According to their obstetric histories, the mothers had not had a serious infection, gastrointestinal or hepatic disease or toxemia. The parents belonged to a group with moderately low incomes, and the majority were followed in the antenatal clinic of the Lying-In Hospital for varying periods prior to delivery. Detailed information on their diets is lacking.

Shortly after death the bodies of the infants were placed in a refrigeration unit. Autopsies were performed on 21 infants and specimens of their livers obtained for analysis within five to seventy-two hours after death. The samples of liver from the remaining 2 infants were obtained four and six days respectively after death. Whenever analysis of the liver for carotene and vitamin A content could not be performed immediately, the tissue was frozen. It was found

that the vitamin A content of livers in the frozen state for four days did not significantly change. It seems unlikely that any considerable loss of vitamin A occurred during the interval between death of the infants and chemical analysis of the livers.¹⁵

CHEMICAL METHODS

Vitamin A and Carotenoids in Blood Plasma.

—The microphotocolorimetric method of May, Blackfan, McCreary and Allen⁶ for determination of plasma carotenoids and vitamin A is especially applicable to studies on small infants. Analyses were made on 1 cc. samples of plasma as follows:

Two cubic centimeters of 95 per cent ethyl alcohol and 2 cc. of petroleum benzene were added, the carotenoids and the vitamin A being extracted in the petroleum benzene layer. The micro unit of the Evelyn photoelectric colorimeter was used with selective color filters, the filter having a maximum light transmission of 440 millimicrons for determinations of carotenoids and of 620 millimicrons for determinations of vitamin A. The conversion of galvanometer readings into arbitrary units was made by the formula of May and his associates.⁶ The terms 440 unit and 620 unit, derived from the filter used in each instance, are used to express the amounts of carotenoids and of vitamin A respectively. These units may be converted into micrograms or U. S. P. units by the following factors: One 440 unit equals 3 micrograms of carotenoids. One 620 unit equals 3 micrograms of vitamin A. One microgram of vitamin A equals 2.85 U. S. P. units. The factor for conversion of arbitrary colorimetric units into micrograms is derived from curves obtained by analysis of pure solutions of beta carotene and crystalline vitamin A; the factor for conversion from micrograms to U. S. P. units is the result of photocolorimetric analyses of solutions of vitamin A standardized in U. S. P. units.¹⁶

Fecal Fat.—Collections were made by scraping the stools from diapers into 50 per cent alcohol. Loss of stool was minimal. Total fat was determined on a sample of dried stool by the method of Tidwell and Holt.¹⁷

15. A. W. Davies (The Colorimetric Determination of Vitamin A by the Alkali Digestion Method, *Biochem. J.* **27**:1770, 1933) found no deterioration of vitamin A content of livers kept at room temperature for three days.

16. Dr. O. Bodansky supplied the latter material.

17. Tidwell, H. C., and Holt, L. E., Jr.: The Estimation of the Total Lipids and the Lipid Partition in Feces, *J. Biol. Chem.* **112**:605 (Jan.) 1936.

13. Navitol-S, a mixture of fish liver oils and vitamin D in mannitan monolaurate, was supplied by E. R. Squibb and Sons.

14. From the obstetric and pathologic departments of the New York Hospital.

Analysis of Livers.—The macrophotocolorimetric method for the determination of the carotenoids and vitamin A content of plasma published by Kimble¹⁸ and already in use in this laboratory was used for the analysis of liver tissue. From 75 to 95 per cent of the whole liver was minced, and 1 Gm. aliquots were weighed, ground to a powder with anhydrous sodium sulfate and shaken for ten minutes with alcohol and petroleum benzene. After centrifugation determination of carotenoids and vitamin A on the petroleum benzene fraction proceeded in the manner described for plasma by Kimble. The photocolorimetric readings indicated only traces of carotenoids.

Analysis of Milk.—Milk and milk products were assayed for carotenoids and vitamin A by

colorimetric units. The average fasting vitamin A level was 11.2 colorimetric units, and the average rise in five hours above the fasting level, 32.1 units. Four infants showed extremely poor absorption of vitamin A in five hours. In the remaining 6 the rise of the plasma level exceeded 29 units, and these infants were therefore considered to be good absorbers of vitamin A. No infant over 21 days of age and weighing more than 2,300 Gm. showed poor absorption.

The age range of the mature infants on the day of the test was approximately the same as that of the premature infants. The average carotenoid level for these infants was 10.2 colorimetric units. Their average fasting vitamin A level was 11.3 units, and the average rise in five hours above the fasting level was 64.6 units.

TABLE 2.—Plasma Carotenoids and Vitamin A Absorption in Infants

Number	Age, Days	Birth Weight, Gm.	Weight on Day of Test, Gm.	Plasma Carotenoids, 440 Units/ 100 Cc.	Vitamin A Levels in Plasma, 620 Units/100 Cc.		
					Fasting	5 Hours	Rise Above Fasting Level
Premature Infants							
1.....	11	1,870	1,680	13.8	31.9	59.8	34.9
2.....	11	2,120	2,300	12.3	7.2	10.5	3.3
3.....	12	2,200	2,500	4.5	3.4	60.6	57.2
4.....	14	2,210	2,270	9.4	12.0*	23.4	8.5
5.....	21	1,526	1,380	4.7	6.7*	8.6	1.9
6.....	21	1,710	1,920	2.5	8.3	12.8	4.5
7.....	28	1,750	2,530	12.9	14.7	60.2	45.5
8.....	45	1,475	2,430	5.7	11.0	68.6	57.6
9.....	60	2,000	3,400	4.0	8.6	50.6	42.0
10.....	60	2,050	4,040	13.9	18.0	83.2	65.2
Average.....	28	1,891	2,490	8.4	11.2	43.5	32.1
Mature Infants							
11.....	6	5,680	2,640	10.0	5.0*	43.4	38.4
12.....	6	5,230	3,140	10.6	7.4*	44.4	37.0
13.....	6	5,740	3,750	14.5	14.4*	24.5	10.1
14.....	6	5,100	4,020	12.1	24.4*	198.9	174.5
15.....	8	3,900	3,300	4.8	8.2*	39.9	31.7
16.....	8	2,030	2,940	3.8	13.6*	27.5	13.9
17.....	17	3,010	3,100	15.4	5.0*	115.0	110.0
18.....	26	4,050	4,410	10.1	7.9	115.0	107.1
19.....	38	3,420	3,880	7.7	11.0	56.2	45.2
20.....	70	3,290	4,460	7.5	16.2	94.6	78.4
Average.....	19	3,845	3,514	10.2	11.3	75.9	64.6

* No vitamin A supplements prior to test.

the method of Kimble¹⁸ after extraction with petroleum benzene in the presence of 95 per cent alcohol.

RESULTS

Vitamin A Absorption Tests.—The results of the vitamin A absorption tests on 10 premature and an equal number of full term infants are shown in table 2. The birth weights of the premature infants averaged 1,891 Gm.; the average of their weights on the day of the test was 2,490 Gm., and their ages ranged from 11 to 60 days. The carotenoid levels averaged 8.4

Only 2 full term infants (no. 13 and no. 16), aged 6 and 8 days respectively, showed poor absorption of vitamin A. Although there was some overlapping, the mature infants as a group showed higher elevations in the plasma vitamin A level at five hours, which indicated more efficient absorption of the vitamin. In both groups the older infants in general showed the higher rises. Maximum elevations were found in the group of mature infants, the rise in 3 infants exceeding 107 units.

The results suggest that both age and prematurity influence the efficiency of absorption of vitamin A.

Table 3 shows the intake, the excretion and the retention of fat in relation to absorption of

18. Kimble, M. S.: The Photocolorimetric Determination of Vitamin A and Carotene in Human Plasma, *J. Lab. & Clin. Med.* 24:1055 (July) 1939.

vitamin A for 8 premature and 2 mature infants. The relation of fecal fat to vitamin A absorption is graphically shown in figure 1. Four premature infants excreted more than 60 per cent of the dry weight of the feces as fat. The feces of the remaining 6 infants contained less than 60 per cent of fat. On the basis of percentage fat in stools, 4 infants were poor absorbers of fat. In general, the infants classified as poor absorbers of fat failed to show good absorption of vitamin A. One infant, classified as a poor absorber of fat, however, retained 81 per cent of the fat of his intake; he may be regarded as having better absorption of fat than would be indicated by the percentage of fat in dry weight of stool. All 6 infants who were good absorbers of fat also absorbed vitamin A well. The results

8 other premature infants at various ages ranged from 2.0 to 33.6 colorimetric units per hundred cubic centimeters of blood (tables 4 and 5).

Weight at birth was not a factor in determining the level of vitamin A (table 4). The mean values for 44 infants who weighed less than 2,000 Gm. at birth and for 45 infants whose birth weights were 2,000 Gm. or more were 11.4 and 12.3 units respectively. A further breakdown into groups of infants not receiving and receiving vitamin A supplements respectively reveals that the smaller infants who received no vitamin A except that contained in milk averaged 8.2 units of vitamin A in the plasma and the larger infants averaged 7.7 units. In the groups which received vitamin A supplements the values for the smaller infants averaged

TABLE 3.—Fecal Excretion of Fat Compared with Absorption of Vitamin A in Premature and Mature Infants

Number	Age, Days	Weight, Kg.	Dietary, Fat, Gm./Kg./Day	Dry Weight of Stools, Gm./Kg./Day	Fecal Fat		Percentage Retention of Dietary Fat	Rise of Vitamin A in Plasma in 5 Hours, 620 Units/100 Cc.
					Gm./Kg./Day	Percentage Dry Weight of Stool		
1.....	11	1.88	5.50	2.02	1.09	54	78	34.9
2*.....	11	2.30	5.12	3.33	2.32	70	55	3.3
3.....	12	2.50	5.17	2.68	1.47	55	72	57.2
5.....	21	1.86	5.12	2.09	1.30	62	76	1.9
6*.....	21	1.92	5.39	3.38	2.40	71	55	4.5
8.....	45	2.44	5.23	1.66	1.01	61	81	57.6
9.....	60	3.40	5.02	1.91	1.03	54	79	42.0
10.....	60	4.04	5.17	0.72	0.34	47	93	65.2
17†.....	17	3.10	4.90	1.17	0.14	37	97	110.0
21†.....	40	2.82	4.86	1.42	0.80	56	84	67.2

* Twin.

† Mature.

‡ Malnourished.

suggest a direct parallelism between absorption of fat and absorption of vitamin A from the intestinal tracts of these infants.

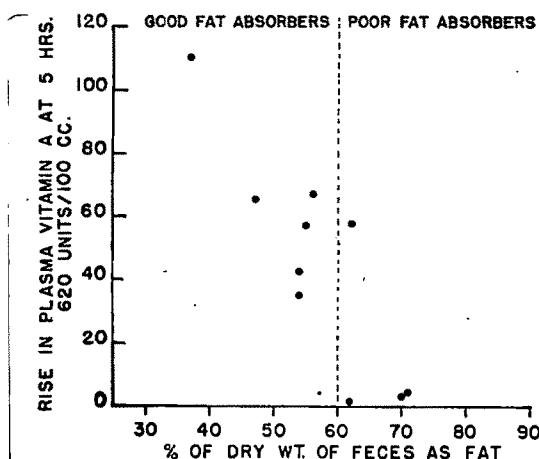


Fig. 1.—Relation of fecal fat to vitamin A absorption.

Vitamin A in Plasma.—Levels of vitamin A in the plasma of 89 premature infants on approximately the twenty-first day of life and of

15.2 units and those for the larger infants 14.4 units.

Regardless of size, there was a significant difference between the 38 infants who received no vitamin A concentrate and the 51 who received various vitamin A supplements, the former averaging 8.0 units and the latter 14.7 units (table 5). Figure 2 shows the distribution of infants with each level of vitamin A in the plasma, arranged in groups according to vitamin supplements received.

Fourteen of the 38 infants receiving synthetic oleovitamin D but no vitamin A supplement had levels between 2.0 and 5.9 units, and no value was above 21.9 units, whereas no babies receiving extra vitamin A had levels below 5.9 units, and 6 were in the higher range (22 to 33.9 units).

A comparison of the effects of the three vitamin A supplements (table 5) revealed a significantly higher mean plasma vitamin A value (17.6 units) for the infants given natural oleovitamin A and D in oil than for those receiving the special mixture containing only one fifth as much vitamin A, the mean vitamin A level of

this group being 13.4 units. Infants receiving the third supplement, navitol-S, which contained approximately the same amount of vitamin A as the first, had the lowest mean level of vitamin A in the plasma (12.1 units). No explanation is at hand for this variation, and too much importance should not be attached to it, inasmuch as the number of babies in each group was small (21, 11 and 19 respectively) and all three groups had values within the range of the normal ones found by Lewis, Bodansky and Haig.³

of livers of the premature group. The values for only 2 of the premature infants exceeded the minimal figures for the full term group. If the averages of the total vitamin A content of the livers of the two groups are compared, it will be seen that the livers of the mature infants contained more than five times as much vitamin A as those of the premature infants. Without exception, the mature infants had more vitamin A stored in the whole liver than was found in the premature infants. These findings indicate

TABLE 4.—*Plasma Vitamin A Level in Premature Infants at Three Weeks of Age*

Supplement	Birth Weight Under 2,000 Gm.				Birth Weight 2,000 Gm. or More				All Cases		
	Number of Cases	Vitamin A 620 Units			Number of Cases	Vitamin A 620 Units			Number of Cases	Vitamin A 620 Units	
		Range	Mean	P. E. of Mean		Range	Mean	P. E. of Mean		Mean	P. E. of Mean
No vitamin A..	24	2.0-17.3	8.2	3.51	14	3.1-20.8	7.7	0.82	38	8.0	0.43
Vitamin A*....	20	7.0-23.0	15.2	3.82	31	6.1-38.6	14.4	0.86	51	14.7	0.58
All cases.....	44	11.4	2.55	45	12.3	0.71	89	11.8	0.43

* 4,500 to 23,000 U. S. P. units of vitamin A daily from third day of life.

TABLE 5.—*Plasma Vitamin A in Infants: Data in Present Study Compared with Those Reported in Literature*

Authors	Subjects				Plasma Vitamin A				
	Infants	Ages	No. of Cases	Supplements *	Range		Mean		P. E.
					U. S. P. Units	620 Units	U. S. P. Units	620 Units	
Present study.....	Premature †	14-23 days	38	No vitamin A	17.1-173.1†	2.0-20.6	68.4†	8.0	0.43
			11	Special	61.6-233.8	7.2-27.7	114.6	23.4	
			21	Oleovit. A and D	59.9-287.3	7.0-33.6	150.5	27.6	0.97
			19	Navitol-S	52.2-193.7	6.1-23.0	103.5	21.1	0.71
			51	All vitamin A	52.2-287.3	6.1-33.6	125.7	14.7	0.58
			89	All cases	17.1-287.3	2.0-33.6	100.9	11.8	0.43
	Premature §	11-60 days	8	Varying amounts	29.1-187.2	3.4-21.9	103.5	12.1	
May, Blackfan, McCreary and Allen °	Mature	6-17 days	7	None	42.8-203.6	5.0-24.4	94.9	11.1	
		26-70 days	3	Varying amounts	67.5-158.5	7.9-16.2	100.0	11.7	
Lewis, Bodansky and Haig °	Full term	4 days to 6 mo.	5	No extra vitamin A	50.4-132.1	5.9-10.9			
			35	No extra vitamin A	45.0-106.0	5.3-12.4†	71.0	8.3†	
			25	17,000 U. S. P. units daily	50.0-151.0	5.8-17.7	93.0	10.9	
			60	All cases	45.0-151.0	5.3-17.7			

* See table 1.

† See table 4.

‡ Calculated: one 620 unit = 8.55 U. S. P. units

§ Table 2, part 1, omitting infants 5 and 6, who are included in table 4).

Carotenoids of the blood plasma in these premature infants ranged from 0.2 to 31.1 units (table 6). No relationship was observed between these values and the levels of vitamin A.

Table 7 shows the vitamin A content of livers of infants who died within the first day. The livers of 16 premature infants contained an average of 48.3 micrograms (138 U. S. P. units) of vitamin A per gram. Those of 7 mature infants averaged 106.3 micrograms (303 U. S. P. units) of vitamin A, over twice the content

that the maturation process plays a role in vitamin A storage, as it does in the storage of iron, calcium and other substances.

COMMENT

The prematurely born infant is handicapped in the neonatal period by relatively low hepatic reserves of vitamin A and impaired absorption of the vitamin from the intestines. These handicaps rarely result in clinical signs of vitamin A deficiency, but they indicate that subclinical de-

iciency may develop quickly if the diet is not supplemented with vitamin A.

The values for hepatic stores of vitamin A reported herein are generally higher than those recorded for premature and mature infants by Wolff,¹⁹ Ellison and Moore,²⁰ Toverud and Ender²¹ and Woo and Chu.²² They correspond more closely to the values of Lewis and others.³ No correlation of storage of vitamin A with fetal age was demonstrated by these investigators. Toverud and Ender found a parallelism between the amount of vitamin A stored in the liver and the carotene and vitamin A content of the maternal diet. It seems likely, however, that fetal reserves of this vitamin are influenced not only by the maternal diet but also, as indicated by the results of the present study, by the maturity of the fetus.

It was anticipated that the defect in absorption of fat from the intestinal tract frequently found in premature infants might be accompanied by poor absorption of vitamin A. The association of inefficient absorption of vitamin A with

and Meserve²⁶ have reported this correlative relation in celiac disease, the celiac syndrome, cystic fibrosis of the pancreas and congenital atresia of the biliary ducts. Minimal elevations of plasma vitamin A in absorption tests occurred only in infants below 3 weeks of age, with maximal rises beyond this age period. This indicates that improvement in absorption of vitamin A occurs as the infants progress beyond the neonatal period. The extent to which absorption of vitamin A is specifically influenced by immaturity of the liver, low plasma lipids and variation in gastrointestinal enzymes and motility was not ascertained in this study.

In the infants studied, levels of vitamin A in the plasma were related to intake of vitamin A

TABLE 7.—Vitamin A Content of Livers of Infants

No.	Age, Hr.	Gestation, Wk.	Body Weight, Gm.	Weight of Liver at Autopsy, Gm.	Micrograms of Vitamin A per Gm. of Liver *	U. S. P. Units of Vitamin A per Gm. of Liver	Vitamin A in Whole Liver, U. S. P. Units
Premature Infants							
1	½	22	720	45	17.0	48	2,160
2	SB†	26	770	42	45.4	129	5,418
3	24	27	850	32	80.7	230	7,360
4	1	25	910	41	15.5	44	1,804
5	7½	24	960	44	36.3	103	4,532
6	6	24	1,030	40	49.7	142	5,680
7	6	24	1,120	44	62.2	177	7,788
8	1	29	1,165	55	52.1	148	8,140
9	SB	29	1,200	78	41.6	119	9,044
10	24	32	1,270	55	33.9	97	5,335
11	9	32	1,375	50	39.5	113	5,650
12	9	31	1,370	52	132.0	376	19,552
13	8	28	1,540	62	48.0	137	8,494
14	SB	32	1,590	80	51.0	145	11,600
15	12	36	1,700	58	19.0	54	3,132
16	SB	..	1,830	76	48.5	138	10,488
Average		26	1,213	53	48.3	138	7,261
Mature Infants							
17	SB	42	2,820	82	140.0	399	32,718
18	SB	40	3,085	145	84.0	239	34,655
19	SB	41	3,160	145	147.0	419	60,755
20	SB	42	3,290	180	65.5	195	35,100
21	20	40	3,320	110	188.0	393	43,230
22	SB	42	3,510	122	78.8	210	25,620
23	SB	42	3,985	180	93.2	266	47,880
Average		41	3,310	138	106.3	303	39,994

* 1 microgram = 2.85 U. S. P. units of vitamin A.

† SB = stillborn.

TABLE 6.—Plasma Carotenoids and Vitamin A in Premature Infants at Age of About Three Weeks

Vitamin A, 620 Units	No. of Cases*	Carotenoids, 440 Units	
		Range	Mean
2.0-5.9	28	0.9-30.1	8.3
8.0-11.9	34	0.2-28.7	9.3
12.0-15.9	20	0.6-31.1	9.6
16.0-32.6	24	1.3-22.1	8.7

* One hundred infants, 6 repeated.

chronic steatorrhea was pointed out by Chesney and McCoord.²³ Breese and McCoord,²⁴ May and associates²⁵ and Spector, McKhann

19. Wolff, L. K.: On the Quantity of Vitamin A Present in the Human Liver, *Lancet* 2:617 (Sept. 17) 1932.

20. Ellison, J. B., and Moore, T.: Vitamin A and Carotene: XIV. The Vitamin A Reserves of the Human Infant and Child in Health and Disease, *Biochem. J.* 31:165, 1937.

21. Toverud, K. U., and Ender, F.: The Vitamin A and D Content of the Liver of Newborn Infants, *Acta paediat.* 18:174, 1935.

22. Woo, T. T., and Chu, F. T.: The Vitamin A Content of the Livers of Chinese Infants, Children and Adults, *Chinese J. Physiol.* 15:83 (Jan.) 1940.

23. Chesney, J., and McCoord, A. B.: Vitamin A of Serum Following Administration of Haliver Oil in Normal Children and in Chronic Steatorrhea, *Proc. Soc. Exper. Biol. & Med.* 31:887 (April) 1934.

24. Breese, B. B., Jr., and McCoord, A. B.: Vitamin A Absorption in Celiac Disease, *J. Pediat.* 15:183 (Aug.) 1939.

25. May, C. D., and McCreary, J. F.: The Absorption of Vitamin A in Celiac Disease: Interpretation of the Vitamin A Absorption Test, *J. Pediat.* 18:200 (Feb.) 1941. May, Blackfan, McCreary and Allen.⁶

and unrelated to birth weight. The average value for premature infants receiving no supplements was 8.0 units (68.4 U. S. P. units). This compares closely with values found by May, Blackfan, McCreary and Allen⁶ and by Lewis, Bodansky and Haig³ for full term infants under 6 months of age that were given no supplement (table 5).

About one-fourth of the premature infants receiving no supplement had levels at 3 weeks of age below 4.5 units (45 U. S. P. units) per

26. Spector, S.; McKhann, C. F., and Meserve, E. R.: Effects of Disease on Nutrition: I. Absorption, Storage and Utilization of Vitamin A in the Presence of Disease, *Am. J. Dis. Child.* 66:376 (Oct.) 1943.

cubic centimeter of plasma. If the criterion of Lewis and others³ is used, levels below 45 U. S. P. units indicate vitamin A deficiency. The infants receiving supplementary vitamin A were all above this level.

SUMMARY

Tests for absorption of vitamin A were performed on 10 premature and 10 full term infants between 6 and 70 days old by determining the rise in plasma level five hours after the ingestion of a test dose. Four premature and 2 mature babies had evidence of poor absorption. The full term infants as a group showed higher elevations in the vitamin A level in the blood plasma after the test dose, and in both groups

were significantly higher in infants who had received vitamin A supplements from the third day of life than in those not given extra vitamin A; about one fourth of the infants in the latter group had levels below that usually considered an acceptable minimum value.

Livers obtained at autopsy from 16 premature and 7 full term infants who died within one day of causes not thought to have affected vitamin A were assayed. Without exception, mature infants' livers contained higher stores of vitamin A than livers of premature babies. The average amount in percentage was more than twice as great in the full term infants, and the amount in the entire liver was more than five times as great.

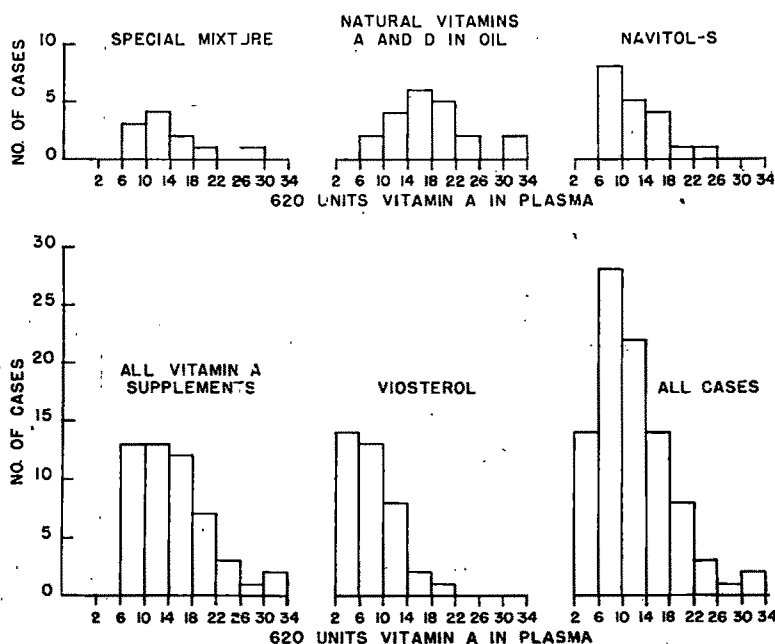


Fig. 2.—Frequency of plasma vitamin A levels in 89 premature infants.

age seemed to favor increased efficiency of absorption.

In 10 infants, 8 of whom were premature, retention and excretion of dietary fat were calculated from assays of fecal fat. In 3 of 4 infants with poor retention of fat, absorption of vitamin A was also poor, while all 6 infants who retained fat well absorbed vitamin A efficiently.

Levels of vitamin A in the blood plasma were determined by a microphotocolorimetric method for 89 premature infants at 3 weeks of age. The average values were of the same order of magnitude as those reported by other investigators for full term babies, but a wider range was found. Birth weight was not a factor in determining the level of vitamin A in the plasma. The levels

CONCLUSIONS

Because premature infants have relatively low reserves of vitamin A in the liver, because they are likely to absorb both dietary fat and vitamin A less efficiently than full term babies and because many premature infants not receiving supplements of vitamin A have low levels in the blood plasma, deficiency of this vitamin may be expected to develop earlier in these infants.

These results suggest that early supplementation of premature infants' diets with concentrates containing vitamin A is a desirable routine procedure.

Mr. George Mladenich rendered technical assistance. Miss Schouten, head nurse of the premature unit, and her staff cooperated in the study.

CONVULSIONS EXPERIMENTALLY PRODUCED IN DOGS

HADDOW M. KEITH, M.D.*; HIRAM E. ESSEX, Ph.D.†
AND CARL F. SCHLOTTHAUER, V.M.D.‡

ROCHESTER, MINN.

The phenomena of fits or convulsions have been observed in human beings and in animals throughout the ages, but the primary cause or causes of such convulsions are as yet not understood. The study of disease produced at will in animals has been in many cases of inestimable value in promoting a clearer understanding of the disease processes in human beings. Numerous attempts have been made to produce in animals changes which lead to convulsive phenomena. Some of these attempts have been eminently successful in producing a single convulsion or a short series of convulsions. The use of insulin, metrazol, thujone, electric shock, strychnine and so forth for this purpose is well known. There is, however, no accepted satisfactory method for producing in animals a series of spontaneous convulsive seizures such as occurs in patients suffering from epilepsy. It was in the hope of discovering such a method that the experiments described in this report were done.

In 1926 Speransky¹ reported the production of convulsions after the freezing of certain areas of the cerebral cortex of dogs. We have performed similar experiments, using the following surgical procedures:

The dogs were anesthetized with ether, and the surgical field was carefully prepared. The skin, fascia and muscles were incised along the parietal and frontal crests and were reflected laterally, exposing the parietal and frontal bones. Enough tissue was left near the midline to make possible easy closure of the incision. An opening through the skull was then made with a trephine over the site selected for a lesion. This opening did not penetrate the dura. A piece of solid carbon dioxide approximately 2.5 cm. in diameter was then placed directly on the dura and was held in place for two minutes. We had learned previously that freezing the brain for only one minute did not produce definite

lesions or convulsions in every instance. Immediately after completion of the freezing, the opening in the skull was closed by replacing the piece of bone removed by the trephine. The bone was merely laid in the opening, and the muscles, fascia and skin were closed in layers over it. Immediately after closure of the wound the dog was permitted to recover from anesthesia and was carefully observed for the first appearance of symptoms.

Lesions were made in various areas of the left cerebral hemisphere. Each lesion was 2 cm. or more in diameter. The lesions in some instances were on or near the cruciate fissure and were definitely in the motor area. However, in most instances they were 2 cm. or more posterior to the cruciate fissure and extended laterally to the ectosylvian or ectolateral fissure. In 21 of the 44 operations the motor activity of each area was determined by direct faradic stimulation immediately prior to freezing.

Twenty-three of the dogs that recovered were operated on again after an interval of twenty-one to two hundred and ninety-seven days. At this time a lesion was made in the right cerebral hemisphere. The same surgical procedures and methods were used as in the first operation.

The results of the 44 operations on dogs can be summarized as follows: 1. Ten animals had convulsions after both the first and the second operation. 2. Nine dogs failed to show symptoms after the first operation but had convulsions after the second. 3. Three dogs failed to show symptoms after either operation. 4. One dog had convulsions after the first operation but not after the second. Of the remaining 21 dogs, which had only a single operation, 11 had convulsions after the operation but 10 did not.

Of the 44 dogs in which lesions of the left cerebral hemisphere were produced, 50 per cent showed symptoms attributable to the lesions and 50 per cent remained free of symptoms. The symptoms noted were similar except in a few atypical cases. Convulsions and epileptiform fits developed and were graded 1 to 4 according to their duration and severity. Two dogs failed to regain consciousness after operation. In all, 20 dogs died within from a few hours to eleven days after the operation. Fifteen of these animals had severe convulsions, and their deaths were directly or indirectly the result of the cerebral lesion.

The convulsions began at varying intervals after the operative procedure, sometimes within

* Section on Pediatrics, Mayo Clinic.

† Division of Experimental Medicine, Mayo Foundation.

Read by title at the meeting of the Central Society for Clinical Research, Chicago, Nov. 5, 1943, and read in full at the meeting of the American Branch of the International League Against Epilepsy, Philadelphia, May 14, 1944.

1. Speransky, A.: Tissue Freezing Procedure for Obtaining Autoneurotoxin and Other Cell Autotoxins: Preliminary Note, *Ann. Inst. Pasteur* 40:213 (March) 1926.

an hour, sometimes only after an interval of nearly twelve hours; most of the animals, however, began to have convulsions within six hours. The seizures recurred over periods of from one hour to thirty-six hours, after which time the animals either succumbed or recovered completely. The seizures were epileptiform, most of them generalized. There were twitching of the muscles of the face, clonic jerking of the legs, champing of the jaws and salivation. These activities were often followed by running movements. In certain animals there were rather localized convulsions, limited to the side of the body contralateral to the lesion.

Necropsy revealed at the site of freezing acute hemorrhagic lesions which had penetrated deeply into the cerebral tissue. In 2 instances there was hemorrhagic exudate in the adjacent lateral ventricle.²

The 23 dogs which were subjected to the second operation now had bilateral lesions in the cerebrum. In these animals the occurrence of symptoms was more frequent after the second operation, and as a rule the convulsions were more severe, than in the interval between the operations. In 19 (83 per cent) of the dogs convulsions and epileptiform fits occurred, whereas after the first operation only 50 per cent of the dogs showed symptoms. The attacks were severe in all the dogs that had convulsions.

The symptoms manifested were in most instances similar to those noted after the first operation, the only difference being that the fits were, in general, more severe and the clonic jerking of the legs was more disorganized. The postoperative time of occurrence of the symptoms varied. In one dog they appeared as early as forty minutes after operation, but in another dog they did not occur until eleven hours and thirty-two minutes after operation. The dogs that recovered did not usually manifest symptoms after the first postoperative day.

The depth of the lesion and the occurrence of subdural hemorrhage appeared to determine the severity of the symptoms. The lesions were deep and penetrating, and subdural hemorrhage was present around them. In the animals that died within a few days after operation bloody exudate was present in the lateral ventricle on the affected side.

Observations were made also on the effect of applying heat, salts and other substances directly

to the cerebral cortex of dogs. In order to test the effect of destroying a small area of the cerebral cortex by heat coagulation, heat was applied to the cerebral cortex of 9 dogs by means of hot running water in a glass applicator containing a thermometer. In 2 animals the brain was heated to from 50 to 60 C. for two minutes; in 3 others the temperature was kept between 75 and 83 C. for two minutes; in the remainder of the series the brain was heated for three minutes to between 72 and 80 C. There were no immediate or delayed convulsive movements in any of the animals. In 1 animal weakness of the right side developed, and another vomited several times. Otherwise no untoward symptoms were noted.

Kopeloff, Barrera and Kopeloff³ in 1942 stated that in monkeys, rabbits and guinea pigs epileptiform fits develop as a result of the placing of aluminum hydroxide cream or of proteins precipitated by aluminum hydroxide cream on the motor area of the brain. These writers found that attacks occur over a period of several months after the initial lesion. We performed experiments on 27 dogs, using aluminum potassium sulfate (alum). At first we placed a small lump of alum beneath the dura of the parietal cortex in 2 animals. Both had severe convulsions and died, 1 in two days and the other in seven. In later experiments it was found that a minimum of 10 mg. of alum per kilogram of body weight was, except in 1 case, sufficient to produce convulsions. The seizures varied from moderate to severe and could be readily controlled by intravenous injection of 5 mg. to 10 mg. of pentobarbital sodium per kilogram of body weight.

Twelve of the 27 dogs in the series of experiments in which potassium alum was used survived for two months or more. Six of these dogs had spontaneous convulsions after being perfectly well for periods varying from two to eight months. Three more of the same group were found dead in their cages under conditions which made presumption of severe convulsions almost imperative: They had been seen to be perfectly well a few hours previously, and the disturbed condition of their cages, their posture and the general appearance of their cadavers were similar to those in cases in which lethal convulsions had been observed. We can say, then, that of the 12 dogs that lived more than two months after the experiments with alum, 50 per cent certainly had spontaneous convulsions; in all probability the percentage was 75. This result is

2. This phase of the subject has been reported by us more fully in another paper (Essex, H. E.; Schlottbauer, C. F., and Keith, H. M.: Symptoms Caused by Experimentally Produced Lesions in the Cerebrum of Dogs, *Am. J. Vet. Research* 5:274 [July] 1944).

3. Kopeloff, L. M.; Barrera, S. E., and Kopeloff, N.: Recurrent Convulsive Seizures in Animals Produced by Immunologic and Chemical Means, *Am. J. Psychiat.* 98:881 (May) 1942.

n confirmation of the work of Kopeloff, Barrera and Kopeloff, although these authors used a different technic for the application of the substance to the cerebral cortex.

In further experiments on dogs the following substances were placed beneath the dura; aluminum sulfate, chloride and acetate; potassium sulfate and chloride and ammonium sulfate; magnesium sulfate and chloride; calcium chloride; and sodium chloride and sulfate. In addition 70 per cent alcohol was injected into the cortical substance. It was found that all of these substances with the exception of magnesium sulfate, magnesium chloride and alcohol produced convulsions in some of the dogs when 15 to 24 mg. per kilogram of body weight was

on cats, whose cortical tissue was frozen in the same manner as has been described for dogs. The results were entirely negative. Symptoms referable to the cortical lesion* were absent. Symptoms did not follow freezing an area of the cortex a second time, contrary to what was so frequently the case with dogs.

Using the same technic as with the dogs, we then performed experiments on 4 monkeys. In these animals we have to date been unable to produce any convulsions, immediate or delayed, either by a first or a second freezing of an area of the cerebrum varying from 22 mm. to 28 mm. in diameter or by application of alum to the surface of the cortex in amounts varying from 10 mg. to 15 mg. per kilogram of body weight.

*Convulsions Experimentally Produced**

Animal	Substance Applied to Brain	Experiments	Results	Comments
Dog	Solid CO_2	44	23 † —11, —10	Two operations; convulsions in 82 per cent of animals after second operation One operation; convulsions in 52 per cent of animals
Dog	Heat, 50-83 C.	9	— 9	No convulsions
Dog	Alum, 5-12 mg./Kg.....	27	—23, — 4	Convulsions in 85 per cent of animals
Dog	Sodium chloride, 25 mg./Kg.....	10	— 8, — 2	Convulsions in 80 per cent of animals
Dog	Calcium chloride, 10-25 mg./Kg.....	5	+ 1, — 4	
Dog	Potassium chloride, 15-25 mg./Kg..	2	+ 1, — 1	
Dog	Alcohol, 3 cc. 70 per cent.....	2	— 2	No convulsions; hyperpyrexia, 115 F., in one animal
Dog	Aluminum hydroxide cream, 2-3 cc.	8	— 8	Immediate convulsions did not occur, but 1 animal died in convulsion 4 months later
Dog	Metallic aluminum powder, 0.3 cc.	2	— 2	No immediate convulsions, but 1 animal had delayed convulsion, from which it died
Cat	Solid CO_2	6	— 6	Neither immediate nor delayed convulsions
Monkey	Solid CO_2	4	— 4	Neither immediate nor delayed convulsions
Monkey	Alum, 10 mg./Kg.....	3	— 3	Neither immediate nor delayed convulsions

* In experiments using a single animal, in each experiment it was found that 15 to 25 mg. per kilogram of body weight of sodium sulfate, potassium sulfate, aluminum sulfate, aluminum acetate, aluminum chloride and ammonium sulfate caused convulsions but that magnesium chloride and magnesium sulfate did not do so.

† Of 23 dogs on which 2 operations were performed, 10 had convulsions after both operations, 1 had convulsions after the first but not after the second operation, 9 had convulsions after the second but not after the first operation and 3 did not have convulsions after either operation.

placed on or in the cerebral cortex. The convulsions occurred as early as thirty-five minutes after the animal recovered from anesthesia or as long as twenty-four hours later. In these experiments 29 dogs were used; 14 of them survived. Eleven of the deaths were thought to be due to the effect of the chemical substance. In 1 case the cause of death was not noted, and in 3 cases distemper was the probable cause.

Two months after the original lesion had been made we attempted to produce convulsions in the surviving dogs by means of stimulation with carbon disulfide applied to the skin at the root of the tail. This produced great excitement, but in no instance were convulsive movements observed.

A limited number of experiments were done in which cats and monkeys (*Macacus rhesus*) were used as subjects. Six experiments were done

The monkeys have been under observation for four months. One monkey showed weakness on the contralateral side after application of alum to the cerebral cortex. In another monkey freezing of an area of the brain 28 mm. in diameter resulted in hemiplegia of the contralateral side.

The results of all the experiments are summarized in the accompanying table.

COMMENT AND SUMMARY

Grossly and microscopically the lesions produced by the application of alum to the surface of the brain are somewhat similar to the lesions caused by freezing. Both are characterized chiefly by edema and hemorrhage, but the lesions produced by freezing are localized and circumscribed, whereas those produced by the local application of alum tend to be diffuse. Not only

does alum destroy the nerve cells with which it comes in contact, but by causing injury of the intima of the blood vessels it also causes distant or remote effects attributable to vascular occlusion. Because of this fact, the lesions produced by alum are chiefly vascular in origin.

Microscopic study of acute lesions produced by the application of alum to the surface of the brain revealed marked edema and capillary hemorrhage. The cells appeared swollen and hydropic, and the intercellular spaces were filled with inflammatory exudate and blood. The intima of the blood vessels was edematous and thickened, and the smaller vessels frequently were occluded by inflammatory exudate. After a few days had elapsed the effects of ischemia were noted. The large nerve cells began to disintegrate and disappear, and only vacuoles remained to mark the places where they had been. The glial cells, being more resistant to effects of ischemia than the nerve cells, tended to survive, and as the nerve cells disappeared the fibrous elements in the lesion tended to contract progressively and to obliterate the spaces left by the nerve cells. The lesion eventually had the appearance of a small mass or band of fibrous tissue. Depending on the size of the original lesion and its site, the healing process caused varying degrees of distortion of the vasodistal framework of the brain—a fact which may account for the occurrence of symptoms many months after the lesion was made.

Convulsions, which were epileptiform, were the chief symptoms produced in dogs by freezing portions of the cerebral cortex. The convulsions were characterized by twitching of the muscles of the face, clonic and tonic spasms of the legs, champing of the jaws and salivation. In some cases the convulsive movements were limited to one side of the body. Running movements were common during the period of recovery. Disturbances of intelligence and sight were not observed. Particularly after the freezing experiments, a latent period between the operative procedure and the occurrence of convulsions was observed. This was sometimes as short as

thirty-five minutes and sometimes as long as eleven and one-half hours.

It is particularly interesting to note that in the animals that recovered the symptoms produced by lesions in the cerebrum caused by freezing did not recur during an observation period of many months. The animals that had the most severe symptoms did not recover. A "status epilepticus" persisted in 1 case for as long as thirty-six hours before the animal died.

It is of interest that heating the cortex to 83 C did not cause any of the symptoms produced by freezing or by chemical irritation or stimulation. Speransky expressed the opinion that the symptoms manifested after the freezing of the cerebral cortex are due to dispersion of toxic product which are formed in the lesion. He stated that animals acquire resistance to this toxic substance. If this were true the effects of a second lesion should be less severe than those of the first, but this is not the case. Our experiments did not therefore, confirm the opinion of Speransky.

Welker and Maslovitz⁴ were unable to find brain proteins in the blood of a large number of the dogs whose brains we had frozen in the manner described. It would appear that if a toxic substance is liberated it is not protein in nature, or at least it is not present in the blood in sufficient quantity to be detected by the effective methods used by Welker and Maslovitz.

To date we have been able to confirm in dogs but not in monkeys or cats, the work of Kopeloff, Barrera and Kopeloff in regard to the production of recurring convulsions by the direct application of alum to the cerebral cortex. We have no explanation as to why freezing and the other procedures described in the present paper produced convulsions in dogs but not in the other animals.

The convulsions produced by the methods described could be controlled in most instances by the intravenous injection of pentobarbital sodium.

4. Welker and Maslovitz: Personal communication to the authors.

Case Reports

INFLUENZAL MENINGITIS IN SIBLINGS

MOSES COOPERSTOCK, M.D.

MARQUETTE, MICH.

In a recent report¹ the occurrence of influenzal meningitis in brothers was described, and the suggestion was made that this disease is potentially contagious, though the condition has not generally been so regarded. The literature had contained only one previous report of influenzal meningitis occurring in siblings.² It has now become established that type B *Haemophilus influenzae* is the causative organism in practically all cases of influenzal meningitis.³ More recently this organism has been found to be responsible also for serious forms of infection outside the central nervous system,⁴ namely, obstructive laryngotracheobronchitis and pneumonia associated with empyema in infants. The multiple occurrence of the latter infections in families in addition to meningitis may point to the potential contagiousness of type B *H. influenzae* infections in general, as indicated, for example, by the 2 instances of acute influenzal laryngitis in the same family mentioned by Sinclair.^{4c}

The following report of an additional instance of influenzal meningitis in siblings may offer further evidence that this serious condition is potentially contagious and may lend support to the suggestion¹ that the institution of prophylactic

measures for the protection of exposed susceptible subjects may be of real importance.

REPORT OF CASES

CASE 1.—M. S., a boy 2 years old, was admitted to the hospital on Sept. 27, 1942. Fever and a chill had developed two days prior to his admission, following mild coryza of approximately one week's duration.

On admission the boy was comatose. His temperature was 103 F. rectally. There was rigidity of the neck and spine. The Kernig and Brudzinski signs were absent. The deep reflexes of the arms and legs were not obtained. The superficial abdominal and cremasteric reflexes were likewise absent. Both ear drums were red and full, and their landmarks were indistinct. The lumbar puncture made on the patient's admission revealed the spinal fluid to be under pressure. The cell count for the spinal fluid was 1,200, with a preponderance of polymorphonuclear neutrophils. The globulin test gave a positive reaction, and sugar was qualitatively absent from the spinal fluid. A direct smear of the spinal fluid and a blood culture on the patient's admission both revealed gram-negative bacilli morphologically characteristic of *H. influenzae*.

The patient was given 3 Gm. of sodium sulfadiazine in 1.5 per cent solution intravenously, followed by 3.2 Gm. in 0.4 per cent solution subcutaneously over a period of twenty-four hours. Marked improvement was noted within twenty-four hours. After the first day sulfadiazine was given by mouth, the patient receiving 6 Gm. daily for one week. The level of sulfadiazine in the spinal fluid was maintained at 20 mg. per hundred cubic centimeters with this dosage. The patient's admission both revealed gram-negative bacilli reaching normal on the third day of hospitalization and remaining within normal limits thereafter. Administration of sulfadiazine was continued in decreasing dosage for an additional three weeks. He made an uneventful recovery.

CASE 2.—N. S., a 3 year old sister, was admitted to the hospital thirteen hours after her brother, M. S. She had had a chill and fever, followed by vomiting, eighteen hours prior to admission.

On admission to the hospital the child was stuporous. Her temperature was 103.2 F. rectally. There was nuchal rigidity and a positive Kernig sign. The left ear drum was injected and moderately full, but the short process was visible. Spinal fluid obtained by lumbar puncture was found to be under increased pressure. The cell count was 3,100. The test for globulin gave a positive result, and the level of sugar in the spinal fluid was decreased according to qualitative examination. A direct smear of the spinal fluid and a blood culture made on admission revealed gram-negative bacilli. Culture of the spinal fluid performed by the division of laboratories of the Michigan State Health

From the Northern Michigan Children's Clinic.

1. Hertzog, A. J.; Cameron, I. L., and Karlstrom, A. E.: *Influenzal Meningitis in Brothers*, J. A. M. A. **124**:502 (Feb. 19) 1944.

2. Davis, D. J.: *Influenzal Meningitis*, Arch. Int. Med. **4**:323 (Oct.) 1909.

3. Pitman, M.: *Variation and Type Specificity in Bacterial Species Haemophilus Influenzae*, J. Exper. Med. **53**:471 (April) 1931.

4. (a) Lemierre, A.; Meyer, A., and Laplane, R.: *Les septicémies à bacille de Pfeiffer*, Ann. de méd. **39**: 97 (Feb.) 1936. (b) Holt, L. E., and McIntosh, R.: *Holt's Diseases of Infancy and Childhood*, ed. 11, New York, D. Appleton-Century Company, Inc., 1940. (c) Sinclair, S. E., with the technical assistance of Fousek, M. D.: *Haemophilus Influenzae Type B in Acute Laryngitis with Bacteremia*, J. A. M. A. **117**:170 (July 9) 1941. (d) Alexander, H. E.; Ellis, C., and Leidy, G.: *Treatment of Type-Specific Hemophilus Influenzae infections in Infancy and Childhood*, J. Pediat. **20**:673 (June) 1942. (e) Alexander, H.: *Treatment of Haemophilus Influenzae Infections and Meningococcic and Pneumococcic Meningitis*, Am. J. Dis. Child. **66**:172 (Aug.) 1943.

Department revealed type B H. influenzae by the direct Neufeld method.

On admission the patient was given 3 Gm. of sodium sulfadiazine intravenously in 1.5 per cent solution, followed by 3 Gm. given subcutaneously in 0.4 per cent solution as an infusion over a period of twelve hours. Thereafter the patient received 6 Gm. of sulfadiazine daily by mouth for three days. The level of sulfadiazine in the spinal fluid with this dosage reached 18.1 mg. per hundred cubic centimeters. On the child's fourth day in the hospital the dose of sulfadiazine was increased to 9 Gm. daily, when the level of sulfadiazine in the spinal fluid had dropped to 8.6 mg. per hundred cubic centimeters. This dosage was gradually decreased after the first week, and use of the drug was discontinued after the twenty-eighth day.

The child's clinical condition improved rapidly after admission, her temperature reaching normal on the third day in the hospital and remaining within normal limits thereafter. She was alert and entirely clear mentally by the third day, and her recovery was uneventful.

COMMENT

In considering prophylactic measures for a family in which type B H. influenzae infection has developed, one would be concerned chiefly with protecting exposed infants and very young children, inasmuch as these infections are prevalent primarily in the early years of life. In one of the most recently reported series of cases of influenzal meningitis 79 per cent were found to have occurred within the first three years of life.^{4e} The high incidence in this age period has been correlated with the low bactericidal properties of the blood against type B H. influenzae which have been found for the same age.⁵

In comparative studies on the protective capacity of the various sulfonamide compounds and of type-specific antibody, Alexander^{4e} and Alexander and Leidy⁶ have shown that sulfadiazine is the superior sulfonamide drug and that it has approximately the same inhibitory power against type B H. influenzae as has type-specific serum. They found the combination of these two agents to be superior to either agent used

singly. As a single effective prophylactic agent sulfadiazine would appear to offer the advantages of ready availability and inexpensiveness when compared with type-specific serum.

While the outcome in the patients described here is of interest as affording instances, additional to those already reported,⁷ of recovery from influenzal meningitis under the influence of sulfadiazine alone, this fact is not necessarily to be regarded as evidence in favor of chemotherapy as a solely adequate method of treatment of this disease. Alexander and her co-workers have demonstrated by experimental studies and clinical results that use of sulfadiazine and serum combined⁸ has the greatest capacity for cure of type B H. influenzae infections and that the use of sulfonamide drugs alone is likely to be therapeutically effective when chemotherapy is initiated early in the course of the disease and when the infection is mild.⁹

SUMMARY

Influenzal meningitis occurred in 2 children in the same family, and they recovered under the influence of sulfadiazine. This report is made primarily as offering further evidence of the contagious potentialities of type B Haemophilus influenzae infections and as indicating the probable importance of prophylactic measures against their occurrence in exposed subjects during the susceptible age period of infancy and early childhood.

7. Alexander.^{4e} Sako, W.; Stewart, C. A., and Fleet, J.: Treatment of Influenzal Meningitis with Sulfadiazine, *J. A. M. A.* **119**:327 (May 23) 1942; Blumberg, M. L.; Tannenbaum, E. L. K., and Gleid, M.: Advances in Chemotherapy of Influenzal Meningitis, *J. Pediat.* **24**:182 (Feb.) 1944.

8. Alexander, Ellis and Leidy.^{4d} Alexander.^{4e} Alexander and Leidy.⁶

9. This statement should perhaps be modified in view of the effect of age. W. Sako, C. A. Stewart and J. Fleet (Treatment of Influenzal Meningitis with Sulfadiazine, *J. Pediat.* **25**:114 [Aug.] 1944) have recently reported a series of cases of influenzal meningitis with a high rate of recovery for older infants and children treated with sulfadiazine alone. They stress, however, the impracticability of employing type-specific rabbit antiserum together with large doses of sulfadiazine in the treatment of young infants.

5. Fothergill, L. B., and Wright, L.: Influenzal Meningitis: Relation of Incidence to Bacteriocidal Power of Blood Against Causal Organism, *J. Immunol.* **24**:273 (April) 1933.

6. Alexander, H. E., and Leidy, G.: Experimental Investigations as a Basis for Treatment of Type B Hemophilus Influenzae Meningitis in Infants and Children, *J. Pediat.* **23**:640 (Dec.) 1943.

HEMOLYTIC STAPHYLOCOCCUS PNEUMONIA IN EARLY INFANCY

RESPONSE TO PENICILLIN THERAPY

ANGUS MCBRYDE, M.D.

DURHAM, N. C.

There have hitherto been no published reports on the use of penicillin in the treatment of pneumonia due to *Staphylococcus aureus hemolyticus* in young infants. The following report of cases is of value because of the ages of the patients, the low dosage of penicillin required to effect recovery and the lack of response to sulfadiazine.

REPORT OF CASES

CASE 1.—A boy aged 5 weeks, whose weight at birth was 2,800 Gm. and whose neonatal course was smooth, one week before his admission to the hospital began to have a slight nasal discharge with considerable nasal obstruction. He had no fever and seemed in good condition until eighteen hours before admission, when he began to vomit his feedings and his condition became rapidly worse. When admitted he was pale and listless but did not appear desperately ill. The infant did not breathe through the mouth. There was a profuse nasal discharge, with marked nasal obstruction which resulted in moderate dyspnea. The throat was moderately injected. There were no abnormal findings in the chest. The leukocyte count was 9,500, with neutrophils 59 per cent (46 per cent segmented, 9 stab, 4 per cent juvenile). The hemoglobin content was 89 per cent. Roentgenograms of the chest showed moderate generalized prominence of the markings of the lungs but no definite areas of consolidation. Cultures of material from the throat showed large numbers of hemolytic staphylococci (*Staph. aureus*).

The infant received sulfadiazine 0.1 Gm. every four hours for twenty-four hours before admission, and administration of the sodium salt was carried on subcutaneously for the first five days in the hospital. The infant's temperature varied from normal to 38.8 C. (102.6 F.). He was placed in an oxygen chamber, the oxygen having been saturated with moisture by passing through boiling water. With each attempt at feeding, the infant became cyanotic and vomited. Twenty-four hours after admission and forty-eight hours after sulfadiazine therapy had been begun he appeared almost moribund. The chest was filled with many fine crepitant rales and a moderate number of coarse rhonchi. Penicillin therapy was begun at this time, with an initial intramuscular injection of 5,000 units, followed by 1,000 units every two hours, so that 41,000 units was given over a period of three days. Six hours after the treatment with penicillin was started, improvement began, and after three days the infant no longer needed oxygen and was able to take feedings by mouth. The thoracic signs disappeared rapidly, and convalescence was uneventful. At the time of writing he is a healthy infant 7 months of age.

CASE 2.—The second infant was admitted to the hospital, at 4 weeks of age, because of pneumonia and inability to be aroused. He weighed 2,600 Gm. at birth and progressed well until 2 weeks of age, when he had an infection of the respiratory tract with pronounced nasal obstruction. When he was last examined by his physician, eighteen hours before his admission, the chest was clear and he seemed in good condition; he was slightly pale but not acutely ill. Nine hours before admission he became lethargic and could not be aroused. On admission the child was dehydrated and slightly cyanotic. He was having considerable difficulty in breathing through the nose, and his respirations were of the Cheyne-Stokes type. The tongue was coated, and the throat was red. There was considerable mucopurulent discharge in the oropharynx. Many fine rales could be heard, especially about the hilus of the right lung. Cultures of the throat taken on his admission showed large numbers of hemolytic staphylococci. No roentgenogram of the chest was taken because of the precarious condition of the infant. Studies of the blood made on his admission showed hemoglobin 74 per cent, leukocytes 14,040 and, neutrophils 65 per cent (segmented 52 per cent, stab 11 per cent, juvenile 2 per cent).

He was immediately placed in an oxygen chamber, with the oxygen passing through boiling water to increase its content of moisture. He was given fluids subcutaneously and intravenously. An initial dose of 0.3 Gm. of sulfadiazine was followed by 0.25 Gm. of the sodium salt every six hours given subcutaneously. This dosage was continued for forty-eight hours without appreciable improvement. Administration of penicillin was then begun, with an initial dose of 5,000 units given intramuscularly, followed by 1,000 units every two hours for two days. On the third day, 1,000 units was given every three hours for a total of 50,000 units. The infant became extremely edematous, so two transfusions of plasma of 50 cc. each were given. Improvement was noted twenty-four hours after treatment with penicillin was begun and after three days the infant was out of danger. The chest signs gradually disappeared, so that four days after the treatment with penicillin was begun no abnormal signs were present. His temperature was 38.8 C. (101.6 F.) on admission and gradually dropped to normal after seventy-two hours. He remained well up to the time of writing, when he was 7 months of age.

COMMENT

The importance of nasal obstruction in acute infections of the respiratory tract in young infants must be stressed. Often the exhaustion produced by dyspnea from nasal obstruction is the main factor in aiding spread of the infection into the tracheobronchial tree. Every effort

From the Department of Pediatrics, Duke University School of Medicine, and Duke Hospital.

should be made to prevent such obstruction, including irrigation of the nasal passage with 0.25 per cent of neo-syneprine hydrochloride or some other shrinking agent, repeated nasal suction and continuous administration of oxygen.

Diffuse inflammatory reaction in the smaller bronchi of infants results in severe dyspnea and cyanosis. Frequently death occurs from asphyxia and toxicity before consolidation of the lungs can be demonstrated. The rapidity with which an apparently trivial infection of the respiratory tract progresses to a desperate illness is illustrated by the brief course of illness of the patients herein described before hospitalization.

Infection caused by pneumococci and by beta hemolytic streptococci usually responds readily to adequate therapy with a sulfonamide compound. Staphylococci are much more resistant to sulfonamide compounds, and death often occurs in a few days even when adequate doses of one of these drugs have been administered. It is my impression that young infants with bronchopneumonia who do not make a dramatic response to such therapy in twenty-four hours

should be treated with penicillin without delay. Cultures should be made, but treatment with penicillin should be started at once without waiting for the report from the laboratory.

SUMMARY

Two instances of hemolytic staphylococcus pneumonia in infants of 4 and 5 weeks respectively are reported.

These 2 patients were given sulfadiazine in adequate dosage for forty-eight hours before treatment with penicillin was started. Their conditions became worse, and though the use of sulfadiazine was continued, the dramatic improvement after penicillin was administered seemed to be due to that agent.

The total amount of penicillin given the 2 infants was 41,000 and 50,000 units respectively. It seems logical to assume that even in severe infections the dosage of penicillin needed for the treatment of young infants is much smaller than that required by older children or by adults.

Duke Hospital.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

THE RESISTANCE OF MENINGOCOCCI TO DRYING. C. PHILLIP MILLER and DORETTA SCEED, *J. Bact.* **47**: 71 (Jan.) 1944.

The authors state that interest in the resistance of meningococci to drying dates back to the observation of Albrecht and Ghon in 1901. Since that time a number of studies have been made. The present one concerns only the duration of viability of meningococci dried in films on various objects (glass beads, pieces of wood and cotton fabrics) under ordinary atmospheric conditions and at room temperature in the dark. Cultures were made each day. Viable meningococci were recovered from glass as long as ten days after drying, and from wood and cotton cloth eight and seven days respectively after drying. The period of survival was shortened at 37 C. and prolonged in the ice box (6 to 10 C.). The virulence of the viable meningococci for mice was not lost. The possible bearing of this observation on the epidemiology of meningococcic meningitis is discussed.

STOESSER, Minneapolis.

GERMICIDAL ACTION OF DAYLIGHT ON MENINGOCOCCI IN THE DRIED STATE. C. PHILLIP MILLER and DORETTA SCEED, *J. Bact.* **47**:79 (Jan.) 1944.

In a previous study the authors showed that meningococci are much more resistant to dehydration than is generally supposed and that they can survive for a week or more in the dark. What is the susceptibility of the organisms to the germicidal action of direct and diffuse sunlight? The question is answered by this study. It was found that meningococci dried in films on the surface of glass, wood and cotton fabric, exposed to different intensities of natural illumination and cultured at intervals to determine the duration of viability were killed by direct sunlight within a very few hours even when protected against overheating. On glass beads and cotton gauze they were killed by diffuse daylight passing through two layers of glass—an ordinary window pane and a pyrex Petri dish—within thirty hours. On cotton toweling and on wood they died a little more slowly.

STOESSER, Minneapolis.

THE ACTION OF DETERGENTS ON STAPHYLOCOCCAL INFECTIONS OF THE CHORIOALLANTOIS OF THE CHICK EMBRYO. T. W. GREEN, *J. Infect. Dis.* **74**:37 (Jan.-Feb.) 1944.

Staphylococcal infections of the chorioallantoic membrane of the developing chick embryo have been used in a survey of the antistaphylococcal action of cationic and anionic detergents. When tested by this method, none of the anionic agents was therapeutically active, while most of the cationic agents did exert a demonstrable therapeutic effect.

Replacement of the chloride or the bromide ion by the iodide ion in several compounds resulted in a lower degree of therapeutic activity. Variation in the length of the carbon chain (12 to 18) in the alkyl groups of a homologous series of compounds resulted in no marked changes in the therapeutic effectiveness.

Because several compounds, very similar in structure and degree of germicidal action, exhibited great differences in effectiveness in the egg, it is concluded that the degree of germicidal action of a compound is not

a sound basis for prediction of relative therapeutic effectiveness even within such a restricted group as the cationic detergents.

The utility of the infected chick embryo as an adjunct in the evaluation of disinfectants is well demonstrated by these experiments. TOOMEY, Cleveland.

HAEMOLYTIC STREPTOCOCCI IN THE DUST OF HOSPITAL WARDS AND THEIR RELATION TO INFECTION. DERRICK G. EDWARD, *J. Hyg.* **43**:256 (Jan.) 1944.

A six months' study of the content of hemolytic streptococci in the dust of one adult and one children's ward was made, and the results were correlated with illness in the wards. The dust from the adult ward for patients with diseases of the nose, throat and eye contained 300,000 hemolytic streptococci per gram, and that from the children's ward, 250,000. About 33 per cent of the organisms in the adult ward were of group A, and 80 per cent of those in the children's ward were of this group. In the children's ward 27.8 per cent of 270 patients were infected with hemolytic streptococci; 12.2 per cent acquired this infection in the hospital.

Sometimes identical cultures were found first in the nose and throat of the child and later in the air. In other instances the order was reversed, which suggests that visitors were the cause of the introduction of these strains.

No conclusive example of hospital cross infection by means of dust was noted, but there was strong suggestive evidence.

JANNEY, Wauwatosa, Wis.

Metabolism; Infant Feeding; Milk, and Other Foods

A REVIEW OF HYPOLYCEMIA, ITS PHYSIOLOGY AND PATHOLOGY, SYMPTOMATOLOGY AND TREATMENT. HAROLD E. HIMWICH, *Am. J. Digest. Dis.* **11**:1 (Jan.) 1944.

This excellent review is most interesting because of the neuropathologic analysis of the five stages in the course of hypoglycemia based on the layers of the brain which are involved. The stages are listed as (1) cortical, (2) subcorticoencephalic, (3) mesencephalic, (4) premyelencephalic and (5) myelencephalic.

The sequence is ascribed to the differences in the metabolic rates in the various regions of the brain, the highest rate being found in the newest portions and each succeeding part possessing a lower rate. Since the area with the most intense metabolic rate will be the first to suffer when energy is withdrawn, the earlier symptoms of hypoglycemia are allocated to the most recent phyletic layers and each succeeding phase is localized according to the decreasing metabolic activity in the subcortical layers. The symptoms of each phase are outlined.

With these five stages as a guide, it is possible to prevent dangerous hypoglycemia by proper treatment on recognition of the initial symptoms. An examination of the patient will reveal his stage of hypoglycemia, and carbohydrate administered at any time before the symptoms of the fifth phase have lasted too long will insure immediate recovery. Any delay after that time will render the prognosis more and more precarious.

MORRISON, Savannah, Ga.

THE RETENTION OF THE NUTRITIVE QUALITY OF BEEF AND PORK MUSCLE PROTEINS DURING DEHYDRATION, CANNING, ROASTING AND FRYING. C. E. POLING, H. W. SCHULTZ and H. E. ROBINSON, *J. Nutrition* **27:23** (Jan.) 1944.

C. E. Poling and others find that the commercial canning process for cured pork shoulder slightly lowers the nutritive quality of the proteins. The proteins of dehydrated pork muscle and fried fresh pork shoulder are slightly superior in nutritive quality to those of canned cured pork shoulder, roast fresh pork shoulder and dehydrated beef muscle.

FREDEEN, Kansas City, Mo.

THE COPPER METABOLISM AND REQUIREMENT OF YOUNG WOMEN. RUTH M. LEVERTON and EMILY S. BINKLEY, *J. Nutrition* **27:43** (Jan.) 1944.

Ruth M. Leverton and Emily S. Binkley found that self-chosen diets of even mediocre quality contained 2.0 to 2.5 mg. of copper, which is the suggested daily allowance for young women. Additional evidence is presented in support of the theory that the body does not excrete copper and that the intestinal tract may deal with copper as it does with iron.

FREDEEN, Kansas City, Mo.

ACTIONS OF BENZEDRINE [AMPHETAMINE] AND PROPADRINE IN THE CONTROL OF OBESITY. M. L. TAINTER, *J. Nutrition* **27:89** (Jan.) 1944.

Tainter concludes from his studies that the effects of amphetamine and propadrine on appetite appear to be the primary explanation of the weight-reducing power of these drugs.

FREDEEN, Kansas City, Mo.

CALCIUM AND PHOSPHORUS ABSORPTION IN BREAST FED INFANTS AND ITS RELATIONSHIP TO BONE DECALCIFICATION (RICKETS). N. L. WAKE, M. J. Australia **1:27** (Jan. 8) 1944.

Ten of 22 breast-fed infants whose source of vitamin D was exposure to sunlight showed defective calcification of the long bones. The differences in mean absorption of calcium and of phosphorus between the infants who showed defective calcification and those whose calcification was normal were not statistically significant. These results lend support to the hypothesis that the amount of calcium stored in the skeleton during prenatal life is the major factor determining the degree of calcification that takes place in the developing bones in the first months of postnatal life.

GONCE, Madison, Wis.

Vitamins; Avitaminoses

BLOOD PLASMA ASCORBIC ACID VALUES RESULTING FROM NORMALLY ENCOUNTERED INTAKES OF THIS VITAMIN AND INDICATED HUMAN REQUIREMENTS. MARY L. DODDS and FLORENCE L. MACLEOD, *J. Nutrition* **27:77** (Jan.) 1944.

Utilization values as determined by Mary L. Dodds and others in the study of daily ascorbic acid requirements of the normal human adult are shown to be close to 1 mg. of ascorbic acid per kilogram of body weight. This amount produced increased plasma ascorbic acid values for all 12 subjects studied; and 3, who had studies of urinary excretion for a thirty day period, reached saturation on such a retention.

FREDEEN, Kansas City, Mo.

INFLUENCE OF INCUBATION AT 37° C. ON STABILITY OF THIAMIN AND RIBOFLAVIN IN COW'S MILK. BARNETT SURE and ZENAS W. FORD, *Proc. Soc. Exper. Biol. & Med.* **54:83** (Oct.) 1943.

When pasteurized cow's milk to which various quantities of thiamine and riboflavin had been added was incubated for forty-eight hours at 37 C. thiamine but not riboflavin was destroyed. Similar results were obtained with raw, untreated milk. Further experiments disclosed that incubating cow's milk for twenty-two hours at 37 C. produces destruction of 46 per cent of thiamine but of no riboflavin. The critical temperature for the destruction of thiamine appears to be between 31 to 37 C. The factors in cow's milk which are responsible for destruction of thiamine are stable to a temperature of 100 C. for ten minutes. The ash of milk produced destruction of 11 to 12 per cent of the thiamine, which indicates that the minerals of milk are responsible for destroying 25 per cent of the thiamine.

HANSEN, Minneapolis.

PRODUCTION OF RIBOFLAVIN DEFICIENCY IN THE MONKEY. HARRY A. WAISMAN, *Proc. Soc. Exper. Biol. & Med.* **55:69** (Jan.) 1944.

Monkeys maintained on a diet free or practically devoid of riboflavin had a "freckled" dermatitis first on the face and then on other parts of the body. This condition developed in from six to eight weeks up to two to three months, depending on the type of diet previously fed. Later definite incoordination of the limbs also developed in the monkeys. The animals became pale and apathetic, and marked decrease in the hemoglobin concentration and in the red cell count was found. Adding biotin to the diet did not affect the dermatitis. Administration of riboflavin caused the dermatitis to disappear in from ten to thirty days, depending on the dose used (50 to 500 micrograms). No evidence of cheilosis or vascularization of the cornea was seen in the monkeys with riboflavin deficiency. The author does not say what happened in regard to the hemoglobin level and erythrocyte count after riboflavin was administered.

HANSEN, Galveston, Texas.

THE VITAMIN C IN THE BLOOD OF SCHOOL CHILDREN. MIGUEL OLIVER and CARMELO FAZIO, *Rev. de hig. y med. escolar.* **2:57**, 1943.

The authors studied the amount of vitamin C in the circulating blood of 113 children whose ages varied from 7 to 14 years, employing Pijoan and Klemperer's technic (titration with 2,6-dichlorophenolindophenol).

The school children, who were healthy in appearance were pupils of the Lainez schools, situated in the poorest districts of Córdoba. Of the 113 children, 59 went to school canteens, in which food is provided by the Parent's School Cooperation Board (Comisión Nacional de Ayuda Escolar). The study was made during the autumn and winter of 1942. The samples of blood were extracted before breakfast, and the estimations were made within two hours. The investigation was completed by questioning the children as to the types of food they consumed daily.

The authors' conclusions were as follows:

1. The general level of vitamin C in the blood of the children studied was good, as shown by the average 1.120 mg. per hundred cubic centimeters of blood.

2. The principal source of vitamin C for the children studied is yerba mate (a South American shrub of whose leaves an infusion is made which is popular in Argentina).

3. There is no significant difference between children who attend school canteens and those who do not as to the level of vitamin C in the blood.

FROM THE AUTHORS' SUMMARY.

Hygiene; Growth and Nutrition; Public Health

THE HURDLE JUMP AS A MEASURE OF THE MOTOR PROFICIENCY OF YOUNG CHILDREN. DORIS M. HARTMAN, *Child Development* 14:201 (Dec.) 1943.

Recent studies have generally supported the concept of specific abilities in the motor area, in contrast to the theory of a general motor ability. However, a study by Cowan and Pratt (*Child Development* 5:107, 1934) reports that motor coordination can be measured by the standard hurdle jump, which would uphold the theory of a general motor ability.

The primary objective in this study was to determine the value of the standard hurdle jump as an indicator of the motor proficiency of the young child. A series of gross motor tests, including the hurdle jump as used by Cowan and Pratt, was administered to 56 children of preschool age. A coefficient of reliability of 0.88, established by retesting, indicated this test to be one of the most reliable measures. In the motor skills tested there was much individual variability in performance. Although the hurdle jump was positively correlated with each of the other tests, the coefficients were not sufficiently high to indicate that the results of this test would predict the other abilities tested. The low intercorrelations further suggest that, while the tests have something in common, different motor abilities have been sampled to a large degree. Multiple correlations were computed for each test with the remaining ones in the battery. The coefficients of correlation obtained indicate that the other tests appear to be as good single indicators of the motor abilities tested in this study as the hurdle jump.

FROM THE AUTHOR'S SUMMARY.

THE PROGRAM OF MEDICAL AND HOSPITAL CARE FOR THE WIVES AND FAMILIES OF ENLISTED MEN. FRED L. ADAIR, *Illinois M. J.* 84:259 (Oct.) 1943.

For the first week ending Nov. 28, 1942, care of only one patient in Illinois was authorized. For the week ending May 1, 1943, 74 applications were approved. With some weekly variation, there has been a steady increase in the number of applications. Many have been rejected because the rules and the regulations state that authorization cannot be retroactive. Up to May 1 the funds obligated amounted to \$48,505.

Care has been authorized for 616 patients of whom 63 have been hospitalized and 53 cared for at home. The number of applications for care of infants has been only 8. The patients have been widely distributed throughout the state, in seventy-two counties. The lowest number in any county was 1, and the greatest was 57.

Fifty-three hospitals and 109 physicians have participated. The greatest number cared for by any one physician is 8. The bills of these hospitals and these physicians have been approved for payment, and some have already been paid.

The extent of the plan cannot be calculated at this time. One cannot foretell its influence on the future practice of medicine and surgery, particularly on that of obstetrics and pediatrics. The plan has the sanction and the support of Congress as a necessity during wartime. It may well set a pattern for postwar practice,

at least for mothers and infants. The medical profession should give it careful consideration and assist in developing a pattern which will be helpful to the patient and the physician alike.

BARBOUR, Peoria, Ill.

THE STATIC AND DYNAMIC PHYSICAL FITNESS OF ADOLESCENTS. J. ROSWELL GALLAGHER, *J. Pediat.* 24:81 (Jan.) 1944.

This report emphasizes the importance of the evaluation and subsequent improvement of various aspects of the physical fitness of adolescent children. Two aspects of physical fitness are considered in detail, static physical fitness, which can be estimated by a medical examination of the usual type, and dynamic physical fitness, which has to do with the physiologic response to brief strenuous exercise.

Data obtained from the initial medical examinations given a group of 910 students at a preparatory school are offered to support the opinion that a careful medical examination should be given members of this age group and that such a procedure is fruitful when it is carefully carried out and when every effort is made to correct the defects which are discovered. A table giving the incidence of abnormalities found at medical examinations of boys belonging to a privileged group is included.

A test of dynamic fitness is described, and the importance of determining the quality of the reaction to brief, strenuous work is discussed. It is emphasized that in the estimation of this aspect of fitness it is necessary to employ an exercise which actually puts the cardiovascular and respiratory systems under stress and that little valid information can be obtained if the exercise used is too mild. The value of using a test for the determination of dynamic fitness is discussed from the standpoint of deciding what is proper exercise for each person and from the standpoint of the evaluation of various programs for physical education.

Prematurity and Congenital Deformities

THE PREMATURE INFANT: MANAGEMENT AND PROGNOSIS. W. R. F. COLLIS, *Brit. M. J.* 1:31 (Jan. 9) 1944.*

Of a small series of premature infants observed by the author 76 per cent developed perfectly, while the other 24 per cent had deformities or difficulties. The author thinks that this is sufficient proof to refute the statement that the majority of premature babies are defective either mentally or physically. He describes the care of premature infants, covering four points that are familiar to all pediatricians: first, the importance of the maintenance of normal body temperature; second, the importance of special technics of feeding, such as gavage; third the importance of special nursing technics, and fourth, the importance of prevention of infection. The only recommendation not followed routinely by most people caring for premature infants is for the use of adrenal cortical extract for the treatment of dehydration. The author says that this treatment has also proved of great value in some instances of shock at birth and in certain instances of dehydration associated with ketosis. The discussion states that there is no doubt that the measures necessary to reduce the death rate for premature infants are elaborate and complicated, but they are well worth while. Because of the high incidence of intracranial hemorrhages, it is advocated that vitamin K be given routinely, particularly to infants with mild toxemia. When a combined effort is made

by obstetricians and pediatricians, a considerable reduction of the incidence of and of the death rates attendant on premature birth should be expected.

BIRDSONG, Charlottesville, Va.

Newborn

PROBLEMS ENCOUNTERED IN EXPLAINING CERTAIN CASES OF ERYTHROBLASTOSIS FETALIS ON THE RH THEORY. AMBROSE J. HERTZOG, Minnesota Med. 26:1057 (Dec.) 1943.

This is a good case report of a baby who died fourteen hours after birth. It was thought to have died of erythroblastosis fetalis of the icterus gravis type. However, the serologic studies did not fall in line with present theories, and the author concludes that, although the majority of cases of erythroblastosis fetalis can be explained on the basis of the Rh antigen-antibody mechanism, other known and unknown factors related to isoimmunization must be involved in those cases that fail to meet the requirements of the Rh theory. The field of isoimmunization is a fertile one for further research and hopeful simplification.

STOESSER, Minneapolis.

ERYTHROBLASTOSIS FOETALIS. GEEHARD J. NEWERLA, New England J. Med. 229:576 (Oct. 7) 1943.

A case of erythroblastosis fetalis with icterus gravis and neonatal anemia in a 9 day old infant is reported, and the recent pertinent literature and theories are briefly reviewed.

Serologic studies substantiated the fact that the Rh factor was at least one of the major causes of the illness. Colostrum was not ingested; hence this cannot account for the liberation of maternal antibodies from the fetal red blood cells in the present case.

Therapeutically, repeated transfusions of blood properly selected and cross-matched, preferably by anti-Rh serum or by Levine's modified technic, are the only successful methods. It should be stressed that Rh-negative blood is important for the infant with erythroblastosis fetalis for at least the first week after birth.

GENGENBACH, Denver.

LARGE TWINS. L. M. PARK, Lancet 1:118 (Jan. 22) 1944.

A case is recorded of twins with a combined weight of 19 pounds 2 ounces (8,705 Gm.), the individual weights being 10 pounds 14 ounces (4,956 Gm.) and 8 pounds 4 ounces (3,749 Gm.).

LANGMANN, New York.

HEMOLYTIC DISEASE IN THE NEWBORN: THE RH FACTOR. F. A. LANGLEY and F. STRATON, Lancet 1:145 (Jan. 29) 1944.

Twenty-one cases of hemolytic disease of the newborn were investigated clinically, pathologically and serologically. In 19 cases an anti-Rh agglutinin was found in the maternal blood.

Of 12 necropsies, 11 showed the medullary hemopoiesis characteristic of hemolytic disease of the newborn.

The breast milk of 10 of the mothers was examined, and 7 samples were found to contain the anti-Rh agglutinin.

LANGMANN, New York.

HEMOAGGLUTINOGEN RH AND ERYTHROBLASTOSIS FETALIS: FIRST OBSERVATIONS MADE IN CHILE. HUGO VACCARO and ARMANDO MEZA, Rev. chilena de pediat. 14:717 (Oct.) 1943.

In an investigation designed to establish statistics on the distribution of the Rh factor, it was found that

92.5 per cent of 172 Chileans selected at random had Rh-positive blood. In 14 cases of erythroblastosis studied, the "classic" Rh relationship—father and infant with Rh-positive blood and mother with Rh-negative blood—was noted.

The authors point out that repeated determination of the maternal antibody titer may have diagnostic value in establishing the Rh status of the fetus in utero; they are carrying out further studies on this point. Premature delivery or delivery by cesarian section is suggested in order to save the infant when erythroblastosis can be fairly prognosticated.

PLATOU, New Orleans.

ERYTHROBLASTOSIS FETALIS AND ITS PATHOGENESIS: CLINICAL OBSERVATIONS ON SIX FAMILIES. ARIZTIA, Rev. chilena de pediat. 14:734 (Oct.) 1943.

Various manifestations of erythroblastosis fetalis were observed and recorded for 14 of 29 infants in 6 families. A fatal reaction occurred after 1 infant with Rh-positive blood received Rh-negative maternal blood. The author enlarges on the pathogenesis of nuclear jaundice (kernicterus), explaining that most of the later neurologic abnormalities are related to neonatal intracranial hemorrhage.

PLATOU, New Orleans.

Acute Contagious Diseases

A PERTUSSIS TOXIN-ANTITOXIN NEUTRALIZATION TECHNIC. MERRITT E. ROBERTS and ANNE G. OSPECK, J. Infect. Dis. 74:14 (Jan.-Feb.) 1944.

Pertussis toxin and toxoid are the best antigens for the production of a potent antitoxic serum.

Pertussis antitoxin can be accurately standardized in vitro toxin-antitoxin neutralization technics. The pertussis antitoxin standard can then be used in all subsequent tests involving the titration of toxins and toxoids.

The neutralization test can be adapted for use in testing the antitoxin titer of human sera.

The lethal effect of a toxic preparation and the necrotic effect produced by the same toxic preparation have been shown to be due to the same toxic principle.

Clinicians should be warned not to be too optimistic as yet.

TOOMEY, Cleveland.

PERTUSSIS ANTITOXIN: ITS RELATIONSHIP TO PROTECTION IN ACTIVELY AND PASSIVELY IMMUNIZED MICE AND RABBITS. ANNE G. OSPECK and MERRITT E. ROBERTS, J. Infect. Dis. 74:22 (Jan.-Feb.) 1944.

A passive protection test is described which differentiates the protective property of antitoxin and that of antibacterial serum in mice challenged with lethal doses of live culture or toxin. The duration of effective passive protection in mice is from four to five days.

Rabbits which are actively or passively protected with antitoxic serum can withstand several lethal doses of toxin or live culture. Most of these protected rabbits will be found to give negative cutaneous reactions when tested with toxin or live culture.

Mice or rabbits which are actively or passively protected with antibacterial serum show little immunity when given challenging doses of toxin or live culture.

TOOMEY, Cleveland.

INFLUENCE OF THE LEVEL OF THIAMINE INTAKE ON THE SUSCEPTIBILITY OF MICE TO POLIOMYELITIS VIRUS. A. F. RASMUSSEN JR., H. A. WAISMAN, C. A. ELVEHJEM and P. F. CLARK, *J. Infect. Dis.* **74**:41 (Jan.-Feb.) 1944.

Mice fed diets deficient in thiamine show a lower incidence of infection to Theiler's virus and to Lansing rain poliomyelitis virus than do animals fed a similar diet with optimum thiamine.

If these thiamine-deficient survivors are subsequently given adequate thiamine, paralysis develops in some of them after a prolonged incubation period.

The decrease in susceptibility noted in mice on diets restricted in caloric value but adequate in all vitamins similar to that observed in thiamine-deficient animals is less marked.

TOOMEY, Cleveland.

THE CLINICAL MODIFICATION OF WHOOPING COUGH BY THE USE OF ALUM-PRECIPITATED DIPHTHERIA TOXOID. J. MUÑOZ TURNBULL and GERARDO VARELA, *J. Pediat.* **24**:46 (Jan.) 1944.

Experimental study led to the following conclusions:

1. The rabbit is better protected with a mixture of pertussis vaccine and alum-precipitated diphtheria toxoid than with pertussis vaccine alone against live *Bacillus pertussis* injected intradermally.

2. Pertussis vaccine alone protects the rabbit if the vaccine is prepared according to the technic of Kendrick.

3. Diphtheria toxoid alone does not protect the rabbit.

Of 54 children with whooping cough treated with diphtheria toxoid precipitated in alum, 37 improved within two weeks after the beginning of the spasmodic cough and 11 within three weeks, while 6 children showed no improvement.

FROM THE AUTHORS' SUMMARY.

THE EFFECT OF RACHITOGENIC DIETS, PARTIAL INANITION, AND SEX ON THE RESISTANCE OF COTTON RATS TO THE VIRUS OF POLIOMYELITIS. H. M. WEAVER, HELEN AMMON and NORMA HASTINGS, *J. Pediat.* **24**:88 (Jan.) 1944.

The results of twenty-one experiments designed to test the influence of rachitogenic diets, partial inanition and sex on the susceptibility and on certain immunologic responses of cotton rats to the virus of poliomyelitis are reported. With two exceptions, each experimental group of animals consisted of 24 cotton rats (6 rachitic and 6 normal males and 6 rachitic and 6 normal females). During the present investigation suspensions of the Armstrong-Lansing strain of the virus of poliomyelitis were injected or instilled in varying quantities into the cecum, stomach, colon, peritoneal cavity, external nares, primary bronchi and blood, beneath the skin of the back and beneath the mucous membranes in the regions which in certain animals other than cotton rats house the palatine tonsils. In addition, the animals of the experimental group were allowed to remain in intimate contact with cotton rats which were dying from the effect of intracerebral inoculation with the virus. Finally each cotton rat of still another experimental group was fed the brain stem and spinal cord freshly removed from a cotton rat paralyzed with poliomyelitis.

Each of the cotton rats which failed to exhibit paralysis after an experimental inoculation with the virus was subjected to three-way reinoculation with the virus at intervals of twenty-five days.

The results of the experiments reported in this communication yield no evidence indicating that avitaminosis D, partial inanition or the sex of the animal affects

significantly the susceptibility of cotton rats to the Armstrong-Lansing strain of the virus of poliomyelitis. Furthermore, there was no indication that the development in cotton rats of resistance to three-way reinoculations with the virus, when the latter were administered subsequent to any of the experimental inoculations, is influenced by avitaminosis D, partial inanition or sex.

AUTHORS' SUMMARY.

DIPHTHERIA IMMUNIZATION. HERBERT W. SWANN, *Brit. J. Child. Dis.* **41**:10 (Jan.-March) 1944.

In 1942 about 50 per cent of all children in Great Britain were immunized against diphtheria (about 35 per cent of those under the age of 5).

As a general rule alum-precipitated toxoid is used, in two injections, of 0.2 cc. and 0.5 cc. respectively.

All children should be given the Schick test about every two years until they reach the age of at least 10 years.

LANGMANN, New York.

POLIOMYELITIS: EXPERIMENTAL WORK IN EGYPT. C. E. VAN ROOYEN and A. D. MORGAN, *Edinburgh M. J.* **50**:705 (Dec.) 1943.

The authors studied 74 cases of poliomyelitis with 19 deaths and 32 cases with 14 deaths occurring in the military forces in the Middle East in 1941 and 1942 respectively. In the native population of 16,000 there were apparently only 11 cases. The authors present in detail clinical, histopathologic and experimental studies on 7 patients who died and from whom 6 different strains of poliomyelitis virus were isolated. Experimentally, the Abyssinian baboon, *Papio hemadryas*, proved to be exceptionally susceptible to infection and was used and recommended by the authors. Inoculation with emulsified spinal cord obtained at autopsy caused reproduction of the disease and death of the animal in three to eight days.

The histopathologic studies are particularly interesting in that they revealed involvement of areas of tissue of which there was no clinical evidence prior to death. Involvement of gray matter from the lumbar area of the cord to the midbrain, with extensive infiltration with polymorphonuclear cells in fulminating lesions and of lymphocytes in nonfulminating lesions was observed. Lesions in the substantia nigra, hypothalamus, cerebral cortex and celiac ganglions are described.

The question is raised as to the possibility that atypical poliomyelitis occurred in 20 patients who had conditions diagnosed clinically as multiple neuritis, radiculitis, syringomyelia, lymphocytic choriomeningitis and encephalitis.

Experimentally the authors found that sodium sulfadiazine failed to prevent or arrest the course of the disease in an inoculated animal.

NEFF, Kansas City, Mo.

THE LABORATORY DIAGNOSIS OF DIPHTHERIA: A NOTE ON SOME PRESENT DAY METHODS. HELEN A. WRIGHT, *Edinburgh M. J.* **50**:737 (Dec.) 1943.

The author states that the biologic distinction between *Corynebacterium diphtheriae* and related nonpathogenic species is not always sharp. Consequently, the diagnosis could be confirmed in only 33 to 55 per cent of the cases reported as instances of diphtheria. Not the clinically well developed but the milder forms cause this problem. False positive reports will be minimized if stained films of organisms grown on Loeffler's medium and of organisms from an eighteen to twenty-four hour culture on a medium containing tellurite are used in combination. There is considerable discussion of the

stains and culture mediums, and of the character of growth. Subculturing of the organism every three to four weeks is recommended in order to maintain characteristic colonies as controls.

NEFF, Kansas City, Mo.

THE PROPHYLAXIS OF SCARLET FEVER IN THE SCHOOL CHILD IN RELATION TO MODERN METHODS OF IMMUNIZATION. JUAN M. MIRAVENT, *Rev. de hig. y med. escolar.* 2:42, 1943.

Recent investigations reported by several North American authors provide new resources for specific prophylactic measures against scarlet fever and a more solid basis for general prophylaxis. However, the improvement of methods of vaccination has not led to a simple solution, which would mean total immunization or at least immunization of the persons who according to the Dick test are most susceptible. All methods, especially those most commonly used, are inconvenient, mainly because of the number of injections (five or more) and because of the reactions to the vaccine which are sometimes severe.

Miravent states that the use of scarlet fever toxoid, common in several countries and recommended by him since 1929, makes immunization easier by reducing the number of injections required and the incidence of reactions. The common practice of giving three doses is approved by the author; this dosage will produce good immunization in most susceptible persons, although not complete in all. Naturally the use of a greater number of doses will reinforce the immunity.

All the author's investigations prove that vaccination against scarlet fever has not yet reached the level, attained by some other vaccinations, which permits discarding of other general prophylactic procedures. It cannot be the basis of prophylactic campaigns, but it is of great importance when because the disease is widely epidemic or exceptionally severe it is necessary to act with more efficiency, disregarding the disadvantages inherent in the method. For these reasons the author prefers the use of attenuated toxin, as he has mentioned in previous papers.

General methods of prophylaxis must be carefully applied according to the circumstances.

With the goal of making all prophylactic campaigns comprehensive and appropriate to the determining causes, the author has investigated some of the particular problems of preventive measures applicable in the schools and the possibilities of carrying prophylactic procedures into the homes.

FROM THE AUTHOR'S SUMMARY.

Acute Infectious Diseases

TREATMENT OF EPIDEMIC DIARRHEAS AND DYSENTERIES IN INFANTS AND YOUNG CHILDREN. KURT GLASER and JAMES W. BRUCE, *J. Pediat.* 24:53 (Jan.) 1944.

A study of different methods of treatment of diarrhea was made by statistical evaluation of the courses of patients admitted and treated at the Louisville General Hospital over a test period of five years (1938-1942).

The types of diarrhea were classified in two groups, one including nutritional diarrhea and the types caused by parenteral infection and the other including the types caused by specific organisms of the dysentery group.

A twelve hour period of starvation, with only water and medicine given by mouth, was started when the patient was admitted to the hospital, with the idea of providing rest for the intestinal tract. Dehydration was combated by oral and intravenous administration of fluid.

Sterile water was forced orally every fifteen to thirty minutes. Solutions of chlorides or of dextrose were given intravenously, as needed, in instances of dehydration. Intravenous administration of plasma or transfusions of blood after reduction of the hemoconcentration, were found highly effective. Sulfathiazole was used in treating the nonspecific types and sulfaguanidine in treating the specific types of diarrhea. Compounds of bismuth and camphorated tincture of opium were used only for patients in whom the infection was resistant to treatment. Polyvalent dysentery antiserum was given to 1 patient.

The dietary measures used deviated from those that are customary. The amount of feeding was neither limited nor forced, and the orders read, for instance "Buttermilk as tolerated," or "Skimmed boiled milk ad libitum." From the statistical tables included in the article the following conclusions could be drawn: (1) The children took large amounts of milk per feeding; (2) the children regulated their intake according to their appetites and without harm to the progress of recovery; (3) when too large amounts were offered, the children limited the intake according to the appetite; and (4) improvement was rapid and recovery occurred earlier than in patients treated by other methods two and more years earlier. The death rate was lower than in previous years.

This form of diet has several advantages. A relatively large caloric intake by the sick and weakened child is achieved by our method in spite of the low caloric value of the foods used. Calculated amounts of this low caloric food would be extremely high, and forcing the intake would be harmful to the condition of the patient. The simplification of the treatment of patients in the hospital and particularly at home, with untrained personnel, is considerable.

The forms of milk used during the test period in 1944 were buttermilk, skimmed boiled milk and protein milk. The use of whole boiled milk, with or without sugar and of formulas made with evaporated milk was abandoned because of the higher amount of dextrose and the slightly laxative effect.

When diarrhea had ceased, as determined by the character of the stools, a gradual return to the normal formulas, by replacing fractions of the average amount of buttermilk taken per feeding, was made.

GLASER, Milwaukee.

PROBLEMS IN MANAGEMENT OF RHEUMATIC DISEASES IN CHILDHOOD. LEO M. TARAN, *J. Pediat.* 24:6 (Jan.) 1944.

The author's studies, based on the natural history of rheumatic disease, bear a realistic relationship to the management of the disease. If the primary aim in treatment is prevention of cardiac damage and prolongation of life expectancy, it seems that the management of rheumatic disease would have to be planned on the basis of the age of the patient and the severity of the infection at the time of the onset of the disease. The younger the child at the time of onset and the more severe the initial attack, the more frequent will be the recurrence, the longer the duration of the active infection and the greater the resultant cardiac damage.

Since rheumatic disease is not reportable, it is in the main outside of the jurisdiction of hospital and health authorities. The care of children with this disease at present is unsatisfactory and fragmentary. It lies in the hands of private institutions, convalescent homes, municipal hospitals and child health agencies, each of which has its own methods and is unrelated in most instances to the other agencies.

The management of this disease demands active mobilization of all public and private agencies concerned with the health and welfare of children. To make such a mobilization effective one must find a method of coordinating all these efforts. Since such coordination does not exist in the present planning for health and welfare, a new approach is warranted.

TARAN, Brooklyn.

THE USE OF SULPHAGUANIDINE IN BACILLARY DYSENTERY. ANGUS E. BREWER, Brit. M. J. 1:40 (Jan. 9) 1944.

Seventy-seven persons with bacillary dysentery were treated with sulfaguanidine. Twenty-six had acute attacks, and 51 had chronic infections. Of the 26 acute attacks, 16 were caused by Shiga's bacillus, 6 by Flexner's bacillus and 4 by unidentified bacilli. Of the 51 chronic infections, 20 were due to Shiga's and 14 to Flexner's bacillus, and the organism responsible for 17 was not determined.

Patients were put to bed, rested and warmed. The frequency and character of the stools were noted, and specimens were plated and examined microscopically. Diet was limited to fluids during the first twenty-four hours. A large intake of fluid by mouth was encouraged in the early stages to replace lost fluid. No intravenous administration of fluid was necessary. Adjuvant treatment was given, patients with Shiga infection receiving 30,000 units of antiserum. A preliminary treatment consisting of colonic irrigations combined with a low residue diet was carried out for 19 patients.

Patients with acute infections received an initial dose of 7 Gm. of sulfaguanidine, followed by doses of 3.5 Gm. at four hour intervals. In severe attacks 3.5 Gm. was given two hours after the initial dose, followed in two hours by 3.5 Gm. more. Usually sulfaguanidine was given until two days after the stools had become normal. Patients with chronic infections received 17.5 Gm. of sulfaguanidine daily, in five doses, for a minimum of eight days, the length of treatment being increased with the severity of the attack. For chronic infections sulfaguanidine must be given until healing of the mucosa has taken place; to gauge this sigmoidoscopy is essential.

Complete cure was obtained in 19 (73 per cent) of the patients with acute infections, in 11 (55 per cent) of those with chronic infections receiving 90 Gm. during six days and in 25 (77 per cent) of those with chronic infections receiving an average of 160 Gm. during ten days. Toxic symptoms occurred in only 9 of the 51 patients with chronic infections and in none of those with acute attacks.

BIRDSONG, Charlottesville, Va.

PROBABLE TETANUS DESPITE INOCULATION WITH TOXOID. R. J. MCGILL, Brit. M. J. 1:40 (Jan. 9) 1944.

Preliminary reports on battle casualties seem to vindicate the administration of two doses of tetanus toxoid at an interval of six weeks. In the British Expeditionary Forces in France and Flanders no tetanus developed in any of the wounded men who had been so inoculated.

One case history reports that tetanus developed in a 20 year old youth who had received tetanus toxoid, but the diagnosis could not be confirmed bacteriologically, the two other possible diagnoses being rabies and poisoning due to strychnine. In the comment the author states that if the patient had tetanus the two protective inoculations had not even sensitized the reticuloendothelial system and the stimulus of the toxin from the wound

produced no increase of antitoxin. He states that, because this is possible, the present practice of giving antitoxin to all wounded men, irrespective of previous inoculation with toxoid, should be continued.

BIRDSONG, Charlottesville, Va.

A CUTANEOUS REACTION TO THE INFLUENZA VIRUSES. W. I. B. BEVERIDGE and F. M. BURNET, M. J. Australia 1:85 (Jan. 29) 1944.

Intradermal inoculation of a 1:10 dilution of unheated or boiled allanotic fluid infected with influenza virus A or B produces a cutaneous reaction in most adults. The degree of the reaction bears no relation to the antibody titer of the serum. Of 31 children similarly tested, 18 had cutaneous reactions, and all of the children but 1 were shown by serologic tests to have been infected in the past by the corresponding viruses. However, many children who had positive reactions to serologic tests failed to exhibit appropriate cutaneous reactions. The suggestion is made that allergy to the virus may play a part in resistance to infection and in the production of symptoms when infection occurs.

GONCE JR., Madison, Wis.

Chronic Infectious Diseases

SENSITIVITY TO TUBERCULIN IN CONGENITAL TUBERCULOSIS. CARLOS A. URQUIJO, Arch. argent. de pediat. 21:38 (Jan.) 1944.

The author studied the sensitivity to tuberculin of 7 infants with congenital tuberculosis who lived thirty-eight to two hundred and forty-five days. Three of the infants did not show positive reactions to tuberculin. The author ruled out, after extensive consideration, the possibility that the lack of response to tuberculin could be the result of a preallergic state or terminal anergy and attributed it to poor sensitivity of the infant's skin.

The absence of a reaction to tuberculin could be related to the strong hydrophilia of the skin of the infant. Tuberculin must stay in contact with the skin during a minimum time in order to cause the characteristic local irritation. The skin is more strongly hydrophilic during the first month of life; therefore the tuberculin enters the general circulation more rapidly. The period of contact being shortened, reaction is apt to be negative or only faintly positive.

The author is aware that this theory is not a complete explanation of the phenomenon, but he states the belief that hydrophilia of the skin plays an important role.

CASSORLA, San Francisco.

Diseases of Blood, Heart and Blood Vessels and Spleen

THE DETRIMENTAL EFFECT OF FREQUENT TRANSFUSIONS IN THE TREATMENT OF A PATIENT WITH HEMOPHILIA. F. L. MUNRO and HAROLD W. JONES, Am. J. M. Sc. 206:710 (Dec.) 1943.

The authors report that in a person with hemophilia who had received numerous transfusions during the past three years the beneficial effect of transfusions has become questionable, and they suggest that they may have become detrimental.

The failure of repeated transfusions to produce any improvement in the condition of a person with hemophilia is described and a possible explanation offered.

HENSKE, Omaha.

AN EVALUATION OF ROENTGEN STUDIES IN HEART DISEASE IN CHILDREN. S. P. DITKOWSKY and EDWIN RYPINO, Illinois M. J. **84**:367 (Dec.) 1943.

In a clinical and roentgen study of 532 children at the Illinois Soldier's and Sailor's Childrer's School the authors found that abnormal cardiac contour denotes cardiac disease but that cardiac disease may exist without producing roentgen changes. Deviation of the esophagus cannot be demonstrated in many children who have evidence of mitral disease. Progressive roentgen studies of the heart offer objective criteria for the evaluation of the status of a convalescent patient. Roentgen examination is an important aid in the diagnosis of heart disease, as the typical auscultatory signs may be absent or overlooked.

BARBOUR, Peoria, Ill.

SECONDARY ANEMIA DUE TO PROLONGED AND EXCLUSIVE MILK FEEDING AMONG SHOSHONE INDIAN INFANTS. M. PIJOAN and C. A. ELKIN, J. Nutrition **27**:67 (Jan.) 1944.

Pijoan and Elkin made their observations on a group of Shoshone Indian infants, who by custom were fed an exclusive milk diet until such time as the child could partake of the regular diet consumed by the adults. The resultant anemia was secondary to the iron deficiency. A modification of Elvehjem's method for determining the iron content of milk was introduced.

FREDEEN, Kansas City, Mo.

DISEASE OF BLOOD IN INFANTS AND YOUNG CHILDREN, INCLUDING THE HEMORRHAGIC STATES. H. G. PONCHER, J. Pediat. **23**:680 (Dec.) 1943.

The broader clinical aspects of diseases involving the blood and the blood-forming organs constitute an important part of the daily practice of every pediatrician. Apart from the well recognized diseases of the blood-forming organs the daily work of the practicing physician in clinical hematology is concerned with well defined reactions to a large variety of stimuli which act on the circulating blood cells or on the blood-forming organs.

While it is true that the general nature of the etiologic agents which affect the blood and the blood-forming tissues of adults and children may be the same, in children the reaction of these tissues may be quite different. This difference is a product of the anatomic aspects and the functional response of the blood-forming organs that are found in childhood. Some of these may be enumerated as follows: (1) wide distribution of the blood-forming tissues, (2) rapid expansion of the blood volume, (3) rapid response of the blood-forming tissues and (4) the nature of the response of immature tissues to certain stimuli, such as infection.

Anemia in infants and children has occupied the major interest of the clinician and the investigator, and most of the progress that has been made has been the result of a more rational understanding of the pathogenesis of this symptom. It is therefore essential that the physician have a practical understanding of the interrelationships of several physiologic processes which are concerned with the maintenance of a normal peripheral blood supply. These processes are the synthesis of hemoglobin, the regeneration of the cellular elements in the blood-forming organs and the maturation of these products, the destruction of blood cells and hemostasis or the maintenance of an intact vascular system.

Anemia during infancy and childhood as well as during any other period of life may result from a dis-

turbance of any one or a combination of two or more of such processes.

Disorders involving the leukopoietic tissues are no as circumscribed as we formerly believed. More frequent use of sternal marrow aspiration has also shown that granulocytopenia may be associated with a hypoplastic, hyperplastic (with maturation arrest) or a dysplastic marrow. The prognosis is more favorable in those cases in which leukopenia and granulocytopenia are on the basis of arrest of maturation if the case is recognized early enough and the causative factor removed to avoid secondary complications due to prolonged depression of the functional elements of defense. Acute leukosis in infants and children may be leukopenic throughout the entire course of the disease, and some of the mononuclear cells often designated as lymphocytes are immature cells of mistaken identity. Study of the sternal marrow in a questionable case of leukosis is a more conclusive aid in diagnosis.

Bleeding from free surfaces or into the tissues may result from a gross deficiency of any single factor or lesser deficiencies in a combination of factors. The factors of clinical importance are the integrity of the capillaries, the composition of the plasma and the quantitative and functional state of the platelets.

The use of standardized laboratory tests will materially aid effective diagnostic evaluation of the patient with hemorrhagic disease.

Clinicians have often expressed the desirability of having an accurate index for the selection of patients with essential or idiopathic thrombopenic purpura who will respond favorably to splenectomy. We have found that the megakaryocytic pattern of the bone marrow as revealed by sternal aspiration offers such assistance when considered with the other symptoms and signs.

Vitamin K as a therapeutic substance has a specific but limited field of use confined to those conditions in which the clinical manifestations are the result of prothrombin deficiency. In cases of extensive damage to the liver the therapeutic value of vitamin K is limited and transient.

Transfusions of freshly drawn blood still remain the treatment of choice in hemophilia. It is not generally appreciated, however, that small amounts of blood are effective in producing mild to moderate prolongation of the coagulation time. When the physician has a person with hemophilia under his care it may be practical to conserve his supply of donors by giving 50 to 100 cc of blood instead of large transfusions unless the latter are indicated because of anemia and reduced volume of blood. Instead of waiting for clinical symptoms of hemorrhage to develop, one may study the coagulation time at routine intervals and give small amounts of blood to keep the rate of coagulation as close to normal as possible.

The recent work on "vitamin P" (citrin) should be closely followed for its place in the management of the hemorrhagic state. As in the case of vitamin K and other factors which play a specific but limited role in the maintenance of the normal hemostatic equilibrium its role will be established only by critical evaluation. Its effect appears to be on the vascular factor and not on the intravascular clotting mechanism.

PONCHER, Chicago.

BLOOD TYPING AND CRITERIA FOR BLOOD-TYPING SERUMS. WILLIAM THALHIMER, J. Pediat. **23**:714 (Dec.) 1943.

1. Blood typing should be performed only with high titered, rapidly acting, standardized anti-A and anti-B serums.

2. The typing serums should be checked at frequent intervals with known type A and type B cells.

3. The blood type ascertained by the use of the red cells of the subject and standardized serums should be checked by testing the subject's serum or plasma with known type A and type B cells.

4. Pretransfusion tests should include direct cross matching of the patient's and the prospective donor's cells and serum or plasma.

5. Pregnant or recently pregnant women with Rh-negative blood who need transfusions should receive only compatible Rh-negative blood.

6. If any person, man, woman or child, has had or is going to need repeated transfusions, one should determine whether his blood is Rh negative or positive. If it is Rh negative, additional transfusions or repeated transfusions are safer if performed only with compatible Rh-negative blood. THALHIMER, New Ycrk.

VASCULAR FRAGILITY AND PERMEABILITY AS INFLUENCED BY VARIOUS AGENTS. GEORGE J. MAJOVSKI, A. J. LESSER, HOMER C. LAWSON, HERBERT O. CARNE and C. H. THIENES, *J. Pharmacol. & Exper. Therap.* **80:1** (Jan.) 1944.

Other observers have noted that certain substances, especially extracts of citrus fruits, lessen capillary hemorrhage in animals. The effective substance was called vitamin P by Szent-György. The present authors found that "when air is suddenly evacuated from a jar in which mice are placed hemorrhage occurred in the lungs of these mice." It was found that a water-soluble extract of lemon peel and crude hesperidin from oranges afforded protection to mice against this hemorrhage for two to four hours after administration, while pure hesperidin increased the bleeding. PILCHER, Cleveland.

PSEUDOTUMOR OF BONE IN HEMOPHILIA. ARTHUR P. ECHTERNACHT, *Radiology* **41:565** (Dec.) 1943.

A case of hemophilia with destruction of a portion of the tibia just distal to the epiphysis simulating a tumor is reported because of its rarity.

A boy aged 13, with a long history of repeated hemorrhages in various joints, causing pain and swelling, was readmitted to the hospital because of a painful swelling over the anterior surface of the left leg below the knee and loss of weight and appetite of three weeks' duration. The temperature was 100 F., and the pulse rate was 102.

The blood contained 10 Gm. of hemoglobin per hundred cubic centimeters and 4,300,000 red cells, 7,700 white cells and 473,760 platelets per cubic millimeter. The differential count was normal. The clotting time was six minutes and the bleeding time two minutes. Kline and Mazzini tests gave negative results. The urine was normal.

Roentgenograms of the left knee showed (1) destruction of the cortex and underlying cancellous bone in the anterior aspect of the proximal third of the tibia, with undermining of the tibial tuberosity, (2) thickening and elevation of the periosteum, with "cuff" formation on the anterior and lateral aspects of the tibia at the level of the lower limits of the overlying soft tissue tumor, (3) deepening of the intercondylar notch of the femur and (4) evidence of subchondral necrosis in the condyles of the femur. The general impression was that of old hemarthrosis or of sarcoma of the tibia.

In addition to roentgen therapy small daily blood transfusions and symptomatic treatments were given. The increase in the size of the tumor was apparently

arrested for a few days, although other hemorrhagic lesions appeared over the body.

The final diagnosis was "large subperiosteal hematoma with massive necrosis of the underlying bone with necrosis and infection of the overlying skin."

Hemophilia may cause subperiosteal hemorrhages with resultant proliferation and thickening of the periosteum, erosion of the underlying cortex and cancellous bone and organization and calcification of the hematoma, producing roentgen changes resembling sarcoma of bone.

Three similar cases from the literature are briefly reviewed. ANSPACH, Chicago.

THE RH CONSTITUENT OF THE HUMAN RED BLOOD CELL. S. D. S. GREVAL and A. B. ROY CHOWDHURY, *J. Indian M. A.* **13:65** (Dec.) 1943.

In a study of 200 Indians in Calcutta, Grevall and Chowdhury found that the Rh factor was present in 90 per cent. The testing serum was prepared from a rabbit. The results were suggestive of a quantitative rather than a qualitative difference. The reactions with 1:10 and 1:25 dilutions of the testing serum indicated that the Rh factor was present in abundance in only 3 subjects (1.5 per cent) and absent from only 2 (1 per cent). In the absence of tests with anti-Rh human serum from isoimmunized mothers, which may give more clearcut reactions, evidence in favor of absolute presence or absence of a new antigen similar to A and B or even to M and N cannot be held to be striking or even inferentially convincing.

GONCE JR., Madison, Wis.

THE RH FACTOR: ITS INCIDENCE IN A SERIES OF VICTORIAN RED CROSS DONORS. R. T. SIMMONS, J. J. GRAYDON, R. JAKOBOWICZ and L. M. BRYCE, *M. J. Australia* **2:496** (Dec. 18) 1943.

Samples of blood from 3,641 adult white persons were examined for the Rh factor by means of the slide technic, a high titer human anti-Rh serum being used; the blood of 643 (17.66 per cent) of these persons was found to be Rh negative. When samples of blood from these persons were retested with 5 other human anti-Rh serums, 20 gave positive results with one or more of the serums. These results indicate that the Rh factor is not a single entity and that different human anti-Rh serums give results, which, although substantially in agreement, show occasional discrepancies. A difference found by the authors between the percentage of subjects with Rh-negative blood in group A and in other groups suggests that the Rh factor may not be entirely independent of the A and B agglutinogens.

GONCE, Madison, Wis.

THE CALCIUM, PHOSPHORUS AND PROTEINS OF THE BLOOD OF SCHOOL CHILDREN OF CORDOBA. HECTOR ORDÓÑEZ FERREYRA, *Rev. de hig. y med. escolar.* **2:65**, 1943.

In an investigation of the amount of protein, calcium and phosphorus in the blood of 100 children from the different quarters of Córdoba who attend Lainez' Schools, the author obtained exceedingly low general averages, especially for total proteins, for which the average obtained was below the minimum accepted as normal. The level of calcium, which was near the minimum normal value, represented a balanced physiologic condition. The general average for phosphorus was low, but none of the values were extreme.

The results indicate that the children tested, who appear to be in good health, have a measurable organic

deficit. This fact was already noted in the comparative stature tables prepared in connection with the statistical study of nutrition.

Values nearest to the normal level were found in children attending school canteens or belonging to families of medium standard of living, which allows them sufficient nourishment. The cost of food of high protein value prevents the lower classes from obtaining it and from giving it daily to their children in the required amount. Thus, lack of nourishment is a primary factor, independent of the other factors, which are worthy of consideration, such as environmental conditions, individual susceptibilities which condition the appetite and pathologic states which may have been overlooked during clinical inspection.

FROM THE AUTHOR'S SUMMARY.

Diseases of Nose, Throat and Ear

THE EFFECT OF DAMAGE TO THE TRACHEAL MUCOSA ON THE DRAINAGE OF RESPIRATORY TRACT FLUID.

ELDON M. BOYD, W. F. PERRY and MARY E. T. STEVENS, *Am. J. Physiol.* **140**:467 (Jan.) 1944.

This paper is concerned chiefly with the part played by ciliary movements in the excretion of respiratory tract fluid. The authors observed that when the ciliated mucosa lining the trachea of rabbits and cats is damaged by inhalation of ammonia or live steam the output of respiratory tract fluid is doubled or tripled when the animals are posturally drained, but drainage is incomplete and at about the normal rate when the animals are not posturally drained. They conclude that other mechanisms besides ciliary drainage are geared to handle not more than the normal load of respiratory tract fluid.

When the output of the fluid in rabbits and cats is doubled or tripled by giving cholinergic drugs or by faradic stimulation of the cervical vagus nerve, this output is not augmented by postural pulmonary drainage, and the ciliated mucosa is undamaged. The conclusion is reached that the ciliary drainage mechanism can handle loads of respiratory tract fluid greater than the normal. In sick cats and dogs with a normal tracheobronchial mucosa but with a congestion of the pulmonary alveoli postural drainage did not help much. In these animals the reserve capacity of the cilia to excrete respiratory tract fluid was great. These laboratory observations should become of clinical value.

STOESSER, Minneapolis.

CLINICAL NOTES: NEW INSTRUMENTS AND TECHNIQS.

USE OF A T TUBE FOR DRAINAGE OF A SEPTAL ABSCESS. FRANCES L. WEILLE and ELIZABETH DE BLOIS, *Arch. Otolaryng.* **39**:85 (Jan.) 1944.

Described in this article is a simple method of draining a septal abscess by the employment of the T tube, well known in the surgery of the bile ducts. A photograph is given of the small T tube which is recommended and of a modification of it for actual use.

GREENWOOD, Chicago.

USE OF CRUDE PENICILLIN IN MEDIA FOR THE ISOLATION OF HEMOPHILUS INFLUENZAE FROM LARYNGEAL CULTURES IN OBSTRUCTIVE LARYNGITIS. LILLIAN BUXBAUM and NICHOLAS F. FIEGOLI, *J. Bact.* **46**: 543 (Dec.) 1943.

The syndrome of laryngotracheobronchitis has been attributed to *Haemophilus influenzae*. The organism has been isolated frequently but often with difficulty. The authors stress the importance of identification of

the causative micro-organism in this disease in order that proper treatment may be instituted. The material removed from the larynx and trachea for bacterial study has been found to contain gram-positive cocci, the overgrowths of which make it difficult to isolate *H. influenzae*. After the publications of Fleming concerning the antibacterial action of filtrates of *Penicillium notatum* it was observed that the addition of crude penicillin to blood agar plates provides a simple but excellent medium for the isolation of *H. influenzae* from the mixed cultures usually obtained from the larynx. The authors obtained typical growths of *H. influenzae* from the penicillin mediums in practically pure cultures. It was found that these cultures could be used without further transplants for serologic identification and for testing the patient's antibody. The suggestion is made that the ease of preparation of these penicillin plates, with stock laboratory mediums used as a base, makes them convenient in a busy diagnostic laboratory.

STOESSER, Minneapolis.

DIADOCHOKINESIS IN STUTTERERS AND NON-STUTTERERS.

CHARLES R. STROTHER and LOIS SMASON KREIGMAN, *J. Speech Disorders* **8**:323 (Dec.) 1943.

Fifteen adult stutterers, 11 men and 4 women, were compared carefully with a control group of approximately the same distribution for sex, dextrality quotient and rhythm. The authors were unable to confirm the previous studies of Blackburn, Rotter, West and Cross; no significant differences between stutterers and non-stutterers were found in respect to rate of diadochokinetic movement of the lips, tongue, jaw or fingers.

PALMER, Wichita, Kan.

THE ETIOLOGY OF STAMMERING: THE PSYCHOPHYSIOLOGIC FACTS WHICH CONCERN THE PRODUCTION OF SPEECH SOUNDS AND OF STAMMERING. ELMER L. KENYON, *J. Speech Disorders* **8**:337 (Dec.) 1943.

The author reviews the psychophysiological facts of laryngeal action and the production of sound and restates his theory that stuttering is a result of compulsory interpolation of normal adduction of the vocal cords when phonation is attempted.

PALMER, Wichita, Kan.

HIGH FREQUENCY DEAFNESS AND DISCRIMINATION OF "HIGH FREQUENCY" CONSONANTS. ROBERT N. PLUMMER, *J. Speech Disorders* **8**:373 (Dec.) 1943.

A test of aural discrimination, involving fifteen so-called high frequency consonants, was administered to 399 college students. From this group 52 persons were selected to represent a scale of distribution from poorest to best. Nine of the 52 students were found to have loss of hearing for high frequencies. Three had general loss of hearing. The 9 persons with loss of hearing for high frequencies had no appreciable difficulty in discriminating between the high frequency consonants; the 3 with general loss did have such difficulty. Discrimination of the sounds of specific consonants did not appear to be dependent on sensitivity to specific frequencies in the higher ranges.

PALMER, Wichita, Kan.

VOWEL QUALITY IN UNSTRESSED SYLLABLES IN AMERICAN ENGLISH. LEE S. HULTZEN, *Quart. J. Speech* **29**:451 (Dec.) 1943.

Vowels in unstressed syllables in English may be treated in three ways: they may be unobscured, partially obscured or fully obscured.

PALMER, Wichita, Kan.

AN EXPERIMENTAL MILITARY SPEECH CORRECTION PROGRAM. SEVERINA E. NELSON, D. P. MCKELVEY, NAOMI HUNTER and MARJORIE WALTER, *Quart. J. Speech* **30**:8, 1944.

Of 682 cadets in the Reserve Officers Training Corps, 12.8 per cent experienced difficulties of speech in the performance of duties in the corps. Most of these reported tired throat or husky voice. The defective groups had lower spirometric measurements than the others. Six hundred and ninety-two additional cadets were tested in an auditorium by two clinicians. Forty-two and eight-tenths per cent had one or more difficulties in speech of a minor sort. During a semester of training in speech 38.2 per cent of those with difficulties of speech showed good improvement.

PALMER, Wichita, Kan.

SPEECH GAMES FOR CHILDREN. DORIS G. YOAKAM, *Quart. J. Speech* **30**:85, 1944.

Parlor games involving speech cost little and interest children greatly in speech. They may be utilized to make drills in speech fun, but they should always be used for the benefits connected with the drills.

PALMER, Wichita, Kan.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

DIARRHEAL DISEASES. GEORGE CALLENDER, *Am. J. Trop. Med.* **24**:7 (Jan.) 1944.

The author discusses briefly the history of diarrheal diseases and the various causes. He also mentions the various types of treatment now employed and prophylactic measures of proved value.

BURPEE, Augusta, Ga.

MEDICAL PROGRESS: PANCREATIC INSUFFICIENCY AND THE CELIAC SYNDROME. SIDNEY FARBER, *New England J. Med.* **229**:653 (Oct. 21) 1943.

The features that characterize the celiac syndrome include typical wasting, more of the limbs than of the face; distention of the abdomen, which may be soft, doughy and inelastic or greatly distended and tight; bulky, foul-smelling, frothy stools that contain excess fat, and often retardation of growth. To these may be added a clumping of barium in the small intestine, a flat dextrose tolerance curve and a low rise in the level of vitamin A in the blood during the vitamin A absorption test. These symptoms may appear as a result of congenital malformation of the small intestine or its attachment, chronic infection, dysentery, megacolon or pancreatic insufficiency. True or idiopathic celiac disease is used to describe this group of symptoms and the laboratory findings in patients in whom no underlying disease can be found and who are improved and usually cured by good general care and any one of the well established celiac diets. Three groups of cases of pancreatic insufficiency are described as follows:

Group 1.—The term "meconium ileus" is used to describe intestinal obstruction in the newborn infant caused by the inability of the intestine to propel through its lumen a thick, mucilaginous meconium, the altered physical state of which is explained by the failure of pancreatic enzymes, particularly trypsin, to act on it during intrauterine life. Death has occurred almost invariably in infants with this severe type of intestinal obstruction. Lesser degrees of obstruction may be produced by inspissated meconium unassociated with pancreatic achylia, as in stenosis of the ileocecal valve. Postmortem examination of patients with true meconium

ileus reveals pancreatic fibrosis with obstruction to the outflow of secretions, proved in some cases to be caused by congenital atresia or stenosis of the main pancreatic ducts.

Group 2.—Andersen found that in the cases of this group the patients usually died before 6 months of age and that many of them presented feeding problems characterized by hunger, failure to gain weight and foul, bulky stools. A somewhat different summary was given by Blackfan and May, who recognized that the clinical manifestations in this group were limited in variety but were common to so many disorders in infancy that a sharply defined clinical picture could not be drawn. Usually, these infants had symptoms referable either to the gastrointestinal tract or to the respiratory system. Vomiting and diarrhea with failure to gain weight or loss of weight preceded the onset of signs of infection of the respiratory system in some cases, but in others a severe and nonproductive cough was an early complaint followed later by a productive cough and physical signs of partial or complete obstruction of different parts of the bronchial tree. Vomiting was usually not present. Diarrhea was occasionally severe and often lasted for prolonged periods. The stools contained no pus or blood and were definitely not fatty. The average duration of the illness of the patients who lived beyond the neonatal period was six months. The average age at death in this group was 8 months.

Group 3.—About half the patients in Andersen's series fell into this group and ranged in age from 6 months to 14½ years. They all died of pulmonary infection. Only one fifth of the patients described by Blackfan and May were included in this group, which possessed clinical features similar to those of true celiac disease, such as emaciation, distention of the abdomen and large, pale, putrefactive, fatty stools. All these patients died of pulmonary disease.

GENGENBACH, Denver.

A TOXIC FACTOR IN TISSUES IN CASES OF NONSPECIFIC ULCERATIVE COLITIS. PAUL E. STEINER, D. WARREN STANGER and MIRIAM BOLYARD, *Proc. Soc. Exper. Biol. & Med.* **55**:8 (Jan.) 1944.

The nonsaponifiable fractions of lungs and livers of various patients, obtained at autopsy, were injected into mice. A toxic factor was present in certain instances, as evidenced by shock, collapse and coma with twitchings and convulsions, usually terminating fatally. Three out of 4 extracts from livers in cases of nonspecific ulcerative colitis were highly toxic, producing shock in every mouse and death in nearly all. Of the 23 extracts from livers of control patients, 16 were nontoxic and 6 were mildly so and 1 (from a cirrhotic liver) killed 3 of 15 mice inoculated (but other extracts from cirrhotic livers were nontoxic). Of the lungs of 3 patients with nonspecific ulcerative colitis, 2 were nontoxic but the third was extremely potent. Fifty-nine control lung extracts were injected into 451 mice with no deaths. The toxic factor was present in extracts from pooled lungs of stillborn infants but not in pooled extracts from the livers of these infants. Attempts were made by the authors to identify the toxic factor, which, it is suggested, is an amine.

HANSEN, Galveston, Texas.

ACUTE GASTRO-ENTERITIS IN CHILDREN: A REVIEW OF 411 CASES, 1936-43, AND A PLAN OF INVESTIGATION AND TREATMENT. WILLIAM GUNN, *Brit. J. Child. Dis.* **41**:1 (Jan.-March) 1944.

The number of recorded deaths in England and Wales from enteritis and diarrheal diseases in children under

2 years of age exceeds the number of deaths at all ages from each of the other chief killing infectious diseases of childhood. A number of causes are doubtless responsible, but the two chief factors are (a) decline in breast feeding and (b) delegation of duties of nursing while the mothers are engaged in war work.

Some of the salient features are:

1. The disease is readily transmissible, and an attack initially mild may prove fatal.

2. Breast-fed babies are not immune, but attacks among them are mild and rarely fatal.

3. The disease is clinically distinct from infections by known intestinal pathogens, for example, dysentery and *Salmonella* organisms, which are rarely fatal.

4. Recognizable infection of the upper respiratory tract is often present, but no special organism is associated, a fact which has led many physicians to postulate a virus as responsible.

5. Mastoiditis is the most frequent and striking morbid change found at autopsy.

6. Initial toxemia and dehydration can usually be corrected, but subsequent progress depends on the presence of an infective focus and the degree of success achieved in dealing with it.

The author advocates a thorough blood and biochemical examination and a bacteriologic investigation of each case.

The two aims in treatment should be (1) to restore metabolism to normal as early as possible; (2) to eliminate or neutralize infection or toxemia.

No specific drugs are available as yet. Sulfaguandine was not found helpful. Sulfasuxidine proved effective in checking excessive fermentation and permitted early administration of dextrose by mouth.

Isolation in single rooms with strict observance of aseptic nursing precautions is considered most important.

LANGMANN, New Ycrk.

Nervous Diseases

MENINGITIS ON THE Isthmus of PANAMA. B. H. KEAN and W. D. CRANDALL, *Am. J. Trop. Med.* **24**:17 (Jan.) 1944.

The authors found 1.14 patients with bacterial meningitis among 1,000 admitted to Gorgas Hospital. Tubercle bacilli were responsible in 29.9 per cent of the cases, pneumococci in 22.9 per cent, meningococci in 22.7 per cent, streptococci in 7.2 per cent, staphylococci in 2.9 per cent, influenza bacilli in 2.7 per cent and mixed organisms in 11.7 per cent. The death rate for all patients was 86.8 per cent. All patients with meningitis caused by tubercle bacilli, pneumococci or staphylococci died. Five per cent of the patients with streptococcal meningitis and 15 per cent of those with influenza meningitis recovered. Fifty per cent of the patients with meningococcal meningitis died.

BURPEE, Augusta, Ga.

CHEMOTHERAPY OF INTRACRANIAL INFECTIONS: II. CLINICAL AND PATHOLOGIC EFFECTS OF INTRACRANIAL INTRODUCTION OF SULFANILAMIDE, SULFATHIAZOLE AND SULFADIAZINE IN NORMAL DOGS. WILLIAM F. MEACHAM, RALPH ANGELUCCI, EDMUND BENZ and COBB PILCHER, *Arch. Neurol. & Psychiat.* **50**:633 (Dec.) 1943.

The authors tested the effect of applying sulfanilamide, sulfathiazole and sulfadiazine to the cortex of dogs. Applications of sulfathiazole produced convulsions with acute pachymeningitis and leptomeningitis and corresponding subacute or chronic inflammation in the later stages, severe fibroplasia in the dura, gliosis and vary-

ing degrees of neuronal degeneration in the cortex proliferation of oligodendroglia and metamorphosis of microglia cells. They suggest that sulfathiazole should not be used in a cranial wound.

BEVERLY, Chicago.

AGENESIS OF THE CORPUS CALLOSUM WITH POSSIBLE PORENCEPHALY. ALEXANDER T. BUNTS and JOHN S. CHAFFEE, *Arch. Neurol. & Psychiat.* **51**:35 (Jan.) 1944.

The literature on agenesis of the corpus callosum is reviewed, and a case in which this anomaly was diagnosed during life by encephalographic means is reported. The patient was a 48 year old man who showed progressive deterioration of the central nervous system.

BEVERLY, Chicago.

EXPERIMENTAL INVESTIGATIONS AS A BASIS FOR TREATMENT OF TYPE B HAEMOPHILUS INFLUENZAE MENINGITIS IN INFANTS AND CHILDREN. HATTIE E. ALEXANDER and GRACE LEIDY, *J. Pediat.* **23**:64 (Dec.) 1943.

The experimental results reported in this paper and the published experience on the results of treatment of influenzal meningitis have established the fact that a combination of sulfadiazine with type-specific antibody is the treatment of choice for infants and children. Nonetheless, publications asserting the sufficiency of the various sulfonamide drugs when used alone continue to appear. These reports fail both to present sufficient data and to include enough cases to warrant conclusions. However, the fact that chemotherapy alone does succeed from time to time indicates a need to examine the matter more closely and to determine, if possible, the circumstances in which the sulfonamide compounds can be relied on and those in which the combined treatment must be used.

It is clear from the results that all the sulfonamide compounds exert a significant inhibitory effect against *Haemophilus influenzae*, both in the test tube and in infected mice. A fairly extensive experience with mouse protection tests for comparison of sulfanilamide, sulfapyridine and sulfadiazine leaves no doubt that the last is the drug of choice among these three.

In vitro tests likewise show that sulfadiazine is vastly superior to sulfanilamide and definitely superior to sulfapyridine, as judged by minimal effective concentrations. Sulfathiazole and sulfamerazine possess an inhibitory capacity approximately equal to that of sulfadiazine.

Sulfadiazine is limited in its power to protect mice when the inoculum exceeds a certain maximum, no matter how high the concentration in the blood is raised. This maximum appears to be 10,000 minimal lethal doses. Serum alone likewise usually fails to protect when the inoculum exceeds this range. When these two agents are combined the mice regularly withstand 1,000,000 minimal lethal doses.

This synergistic effect of the two agents appears to be essential in the treatment of severe meningitis due to type b *Haemophilus influenzae* in infants and children. When the infection is judged mild, as indicated by a concentration of dextrose in the spinal fluid of 40 mg or more per hundred cubic centimeters, and when the clinical features are in keeping with this, the use of sulfadiazine alone is justified initially. The authors' experience suggests that the simple in vitro test described may be of value in determining the susceptibility of a given strain to sulfadiazine. If these tests indicate satisfactory inhibition, as judged by the minimal effective concentrations, it is believed that use of the drug

alone may be continued without risk, provided that clinical improvement ensues and provided that examination of the spinal fluid shows the infection to be under control, with cultures sterile forty-eight hours after the start of chemotherapy.

Two points deserve emphasis. A longer period of therapy with the sulfonamide compound appears to be necessary, if recovery is to be complete, when sulfadiazine alone is used than when rabbit antibody is used in addition. When both agents have been used it has been the policy of the authors to discontinue the administration of sulfadiazine one week after sterilization of the spinal fluid, provided the chemical and cellular constituents of the fluid are in the normal range, the culture remains sterile and the clinical improvement parallels the laboratory results. If sulfadiazine is used alone, this period should probably be extended to two weeks. The initial improvement seen so frequently following the use of sulfonamide compounds can be misleading. The patient may seem to be better, judged either clinically or by changes in the spinal fluid. The number of cells shows a striking decrease, content of sugar rises and the organisms are not seen in stained smears; but the use of satisfactory culture mediums yields growth of the organisms and thus demonstrates that the infection remains active. We have seen many examples of such a course.

The criteria suggested for selection of patients suitable for treatment with sulfadiazine alone are as follows:

1. The treatment must be started early in the course of a mild infection.
2. The strain of type b H. influenzae causing the infection must be shown to be sensitive to sulfadiazine.
3. The spinal fluid should be sterile forty-eight hours after administration of sulfadiazine, and frequent examinations of the spinal fluid must demonstrate that it remains sterile, and that the sugar content of the spinal fluid is maintained above 40 mg. per hundred cubic centimeters. If sulfadiazine alone fails to accomplish these ends, type b H. influenzae rabbit antiserum should be administered.

ALEXANDER, New York.

THE ETIOLOGY OF CONGENITAL CEREBRAL PALSY.
HERMAN YANNET, J. Pediat. 24:38 (Jan.) 1944.

A statistical analysis of data for various pertinent factors obtained from the histories and examinations of 86 patients with congenital cerebral palsy was carried out. The following observations were made:

1. The average age of the mother at the time of birth of the affected child is significantly greater than that found in the general population.
2. The affected children tend to have a later ordinal birth rank than would be normally expected.
3. There is a significant incidence of similarly affected siblings of patients with cerebral palsy.
4. The incidence of mental deficiency in the non-affected siblings is greater than would be expected from random selection.
5. There is an unusually high incidence of associated physical defects, especially those involving the eyes, in patients with cerebral palsy.

It was suggested that these and associated observations can best be reconciled with the conception that developmental cerebral malformations, of which a proportion may be genetically determined, are of primary importance in the causation of cerebral palsy. In support of this contention there were pointed out certain similarities between the results of this study and those of studies of congenital defects and malformations.

FROM THE AUTHOR'S SUMMARY.

A CONTRIBUTION TO THE PATHOLOGY AND THERAPY OF DYSARTHRIA DUE TO CERTAIN CEREBRAL LESIONS.
EMIL FROESCHELS, J. Speech Disorders 8:301 (Dec.) 1943.

The disorders of speech resulting from various lesions of the nervous system, both peripheral and central, are described. Analysis is made of the functions of the various organs of speech in paresis and paralysis. Various corrective technics are described, and illustrative cases are presented.

PALMER, Wichita, Kan.

Psychology and Psychiatry

MODERN APPROACH IN THE STUDY OF APHASIA. G. K. YACORZYNSKI, J. Speech Disorders 8:349 (Dec.) 1943.

Four fallacies prevalent in the study of aphasia are discussed: (1) emphasis on strict cerebral localization, (2) classification of symptoms rather than study of functions, (3) inadequate observation and (4) theoretical bias.

In subjects with unilateral lobectomies, by adequate objective tests, the following phenomena were observed: 1. The threshold of perception was affected so that it took a longer time for the person to apprehend a situation. 2. The number of features which could be perceived in a situation was below normal. 3. The ability to shift from one stimulus to another was decreased. 4. The ability to perceive logical relationships between objects deteriorated.

Further progress in the reeducation of persons with aphasia must rely on a newer knowledge of the mechanisms which underlie the production of speech.

PALMER, Wichita, Kan.

THE BRUSH FOUNDATION STUDY OF CHILD GROWTH AND DEVELOPMENT: I. PSYCHOMETRIC TESTS.
ELIZABETH EBERT and KATHERINE SIMMONS, Monograph of the Society for Research in Child Development, 1943, no. 8.

An analysis of psychometric data collected during a ten year study of children aged 2 to 15 years is presented. Most of the children were of North European ancestry and came from families which were superior economically and educationally. The report covers chiefly (1) cross-sectional and longitudinal analyses of scores in intelligence as determined by the Stanford-Binet test, 1916 and 1937 revisions, and the Otis S-A tests, (2) an analysis of scores in nonverbal intelligence or performance as determined by the Merrill Palmer scale, the Kent-Shakow form board, the Kohs-Kent block designs and the Minnesota paper form board, (3) an evaluation of results of psychometric tests in predicting scholastic achievement at both junior and senior high school levels, scholastic achievement having been determined by the progressive achievement test (intermediate and advanced batteries) and (4) the data for standardization of results of the Kent-Shakow form board test.

Longitudinal analysis of the results of the Stanford-Binet test revealed greater variability in boys than in girls, insignificant differences between age means for boys and for girls, and significantly large proportions of boys and of children with mothers who were college graduates among those making the largest gains in intelligence quotient. The test-retest correlations were positively correlated with the percentage of overlap of the mental ages; scores for the 1937 revision showed changes of 0 to 5 points in the intelligence quotients of 50 per cent of the group when the standard deviations

of the mean mental age at the two ages were similar. Substantial predictability was found in the results of the performance tests. The preschool Merrill Palmer test should definitely be classified among the tests of "mental manipulation of spatial relations" rather than with the Binet test. The predictability of scholastic achievement on the basis of scores on earlier intelligence tests agreed closely with the self correlations of scores on intelligence tests over equal intervals.

FROM THE AUTHORS' SUMMARY.

A SIX-MONTH REPORT ON THE PERSONALITY DEVELOPMENT OF A THIRTEEN-YEAR-OLD STUTTERING BOY. NELL WILL, *Quart. J. Speech* 30:88, 1944.

The author describes a six month program of retraining for a stutterer, a boy 13 years old. Correction was approached by considering the child in his total environment; he was made to feel worthy and intelligent, given exercises for relaxation and told to think about the objects he was speaking about. He was allowed to listen to a record of a normal child hesitating over and over again, and he was told not to care if he did have hesitations. The parents, teachers and others in his environment were spoken to, and the child was encouraged to talk to these people about his stuttering. Nine of them complimented the child when he was relaxed and easy and also attempted in various ways to give him a normal situation. Apparently he adjusted in speech to the point where he was almost as fluent as a normal speaker, and his general adjustment in all directions improved.

PALMER, Wichita, Kan.

Diseases of the Ductless Glands; Endocrinology

MODE OF ACTION OF THIOUREA ON THE THYROID GLAND OF RABBITS. EMIL J. BAUMANN, NANNETTE METZGER and DAVID MARINE, *Endocrinology* 34:44 (Jan.) 1944.

Administration of thiourea caused hyperplasia of the thyroid gland in rabbits and a rapid decrease in both thyroxin and nonthyroxin iodine. The iodine was promptly excreted in the urine. The inhibition of the formation of thyroxin indicates that thiourea produces functional thyrostatics of the thyroid cells.

JACOBSEN, Buffalo.

QUANTITATIVE STUDY OF THE EFFECTS OF ESTRADIOL BENZOATE AND PROGESTERONE IN MODIFYING THE INCIDENCE OF BINUCLEATED CELLS IN THE RABBIT LIVER. JOHN C. ALLAN, *Endocrinology* 34:50 (Jan.) 1944.

Owing to the fact that the liver normally contains a large number of binucleated cells, it was thought that the incidence of these cells might prove to be of value in assessing the activity of estrogen and progesterone, as these hormones are known to cause nuclear changes in the cells of the uterus and vagina.

It was found that with physiological concentrations there was a direct relationship between the amount of estradiol benzoate and progesterone administered and the incidence of binucleated cells.

Whether the liver activates or excretes estradiol benzoate and progesterone, the activity is not achieved without affecting the nuclei of the hepatic cells.

JACOBSEN, Buffalo.

CRETINISM IN RATS INDUCED BY THIOURACIL. A. M. HUGHES, *Endocrinology* 34:69 (Jan.) 1944.

Continued administration of thiouracil to rats from the time of birth resulted in seriously retarded growth,

arrested development, mild anemia and changes similar to those seen in cretinism.

If thyroxin was given concurrently these effects were not observed.

JACOBSEN, Buffalo.

EFFECT OF LOW POTASSIUM DIET AND DESOXYCORTICOSTERONE ON THE RAT HEART. DANIEL C. DARROW, *Proc. Soc. Exper. Biol. & Med.* 55:13 (Jan.) 1944

From study of 26 rats it was found that, whereas a diet low in potassium caused little decrease in the potassium in heart muscle, the simultaneous administration of desoxycorticosterone caused a definite decrease of the potassium in heart muscle. The sodium content was increased, while the water content remained the same. The author warns that if a patient is on a diet low in potassium or is given considerable dextrose by infusion the administration of desoxycorticosterone acetate may actually lead to loss of muscle potassium.

HANSEN, Galveston, Texas.

Skin Diseases; Allergy

TREATMENT OF ACNE VULGARIS WITH COMEDOS BY MONOTERMAL ELECTRODESICCATION. REUBEN NOLAND, *Arch. Dermat. & Syph.* 48:302 (Sept.) 1943.

Destruction of comedos and milia by monopolar electrodesiccation was carried out in 31 patients with various types of acne who had not responded to simple treatment. Excellent results followed in 25 patients. The best results were obtained in the mild acne of adolescents and in the superficial type seen mostly in women in their midtwenties.

Persons with acne conglobata did not respond, but patients with less severe eruptions responded well, particularly when desiccation was combined with roentgen treatment; a method which was used for 7 patients.

JACKSON, Iowa City.

SODIUM PROPIONATE IN THE TREATMENT OF SUPERFICIAL FUNGUS INFECTIONS. EDMUND L. KEENEY and EDWIN N. BROYLES, *Bull. Johns Hopkins Hosp.* 73:479 (Dec.) 1943.

Since sodium or calcium propionate incorporated in bread dough inhibited the growth of molds, the authors prepared an ointment, a solution and a powder containing 10 per cent of sodium propionate and used them for the treatment of a variety of conditions caused by common fungi. No evidence of irritation or toxicity was observed, and the treatment appeared to be effective.

LYTTLE, New York.

THE EFFECT OF SODIUM, POTASSIUM AND THIOSULFATE IONS ON ANAPHYLAXIS. ROBERT G. CARLSON and RICHARD W. WHITEHEAD, *J. Allergy* 14:462 (Sept.) 1943.

Guinea pigs were sensitized to sheep serum. A shock dose was given two to four weeks after the sensitizing dose. The minimum lethal dose of serum was determined. The effect of sodium thiosulfate, potassium chloride and potassium thiosulfate was tested by mixing the salts with the antigen or giving them before the administration of the serum.

Sodium thiosulfate showed no inhibitory effect on the anaphylactic reaction.

The potassium salts showed some value in preventing death. There was no difference in the effects of potassium chloride and potassium thiosulfate.

HOYER, Cincinnati.

PLASMA TREATMENT OF SEVERE, NEAR-FATAL ANAPHYLACTIC SHOCK. ARTHUR H. RAYNOLDS, J. Allergy **14**:495 (Sept.) 1943.

"1. A report is presented of a case of severe, near-fatal anaphylactic shock of 'exudative' type (excessive blood volume loss).

"2. The intravenous use of plasma, now increasingly available, may prove to be a specific treatment for this alarming condition. It should be tried early and in adequate amounts."

HOYER, Cincinnati.

THE ABSORPTION OF WHOLE RAGWEED POLLEN FROM THE GASTROINTESTINAL TRACT. R. HECHT, M. M. MOSKO, J. LUBIN, M. B. SULZBERGER and R. L. BAER, J. Allergy **15**:9 (Jan.) 1944.

"1. The absorption of pollen allergen from the gastrointestinal tract was studied by means of the reactions produced in passively sensitized skin sites.

"2. The appearance of the reaction varied, some giving reaction and some not. The results suggest that there is a relationship between the acidity present in the stomach at the time of ingestion of the pollen, and the absorption of the pollen allergen.

"3. Artificial elevation or reduction of gastric acidity by oral administration of acids or alkalis tends to decrease or respectively increase the absorption of orally administered pollen allergen."

AUTHORS' SUMMARY.

THE EXPERIMENTAL USE OF ETHYLENE DISULFONATE (ALLERGOSIL BRAND) IN THE PREVENTION OF ANAPHYLAXIS IN GUINEA PIGS. ROY T. FISK, WILLARD S. SMALL and ALVIN G. FOORD, J. Allergy **15**:14 (Jan.) 1944.

Ethylene disulfonate is one of many substances suggested for the treatment of bronchial asthma. Several investigators have reported it to be effective in the prevention of anaphylaxis.

Because of a great difference in the death rate of control animals in experiments reported previously by other investigators, the authors performed the present study. They concluded that ethylene disulfonate does not produce a significant degree of protection against anaphylactic shock.

HOYER, Cincinnati.

FAILURE OF VITAMIN E IN THE TREATMENT OF RAGWEED POLLINOSIS (HAY FEVER). JEROME GLASER and HENRIK DAM, J. Allergy **15**:18 (Jan.) 1944.

Ephynal acetate, synthetic vitamin E, was given to 28 patients with hay fever during the season of exposure in 1942. The results were compared with those obtained by the administration of pollen extracts and symptomatic remedies to the same persons the previous year and to a group of controls the same year.

The authors feel that synthetic vitamin E has no value in the treatment of pollinosis due to ragweed.

HOYER, Cincinnati.

POTENTIAL POLLINOSIS IN A DESERT AND A COASTAL CITY: A COMPARATIVE BOTANIC SURVEY OF BARSTOW AND SANTA ANA, CALIFORNIA. R. W. LAMSON, H. MCMICHAEL and M. STICKLER, J. Allergy **15**:21 (Jan.) 1944.

The authors present a comprehensive article pertaining to the vegetation in and around Barstow and Santa Ana.

The survey extended over a period of eight years and shows that the flora may vary from year to year. Studies were made during different seasons.

HOYER, Cincinnati.

TREATMENT OF SCABIES WITH AN EMULSION OF ROTENONE. E. P. WOODROW, South African M. J. **17**:233 (Aug. 14) 1943.

The author reports excellent results in the treatment of 225 patients with scabies with an emulsion of rotenone. Of the 177 patients who returned for observation, all except 10 were cured by one course of treatment. Of the 10 who relapsed, 9 were cured after one further course of treatment, and the tenth required a third course. The solution used on all infants under 9 months of age and on many adults with mild infestations consisted of 1 per cent rotenone and 3 per cent chloroform in mucilage of chondrus. For severe infestations in adults the percentages of rotenone and chloroform were doubled. The lotion was applied twice the first day and twice the second, a bath being taken before the initial application but not again until the third day.

GONCE, Madison, Wis.

Surgery and Orthopedics

TEMPERATURE IN SHOCK. J. DEVINE, M. J. Australia **2**:476 (Dec. 11) 1943.

After trauma to the hindlegs of dogs the increase in volume of the warmed limb was over three times that of the cooled limb. The logical clinical application of this observation is that, firstly, heat should not be applied in the neighborhood of injuries that are likely to cause shock, for if this is done local loss of circulating fluid to the tissues will be increased, and, secondly, cooling of a traumatized limb may be effective in lessening the local loss of fluid from the circulation and may thus be helpful in modifying the onset of shock.

GONCE, Madison, Wis.

BURNS IN CHILDREN. H. E. GIGLIO, Rev. Soc. pédiat. de la Plata **4**:87 (Dec.) 1943.

The first steps in the treatment of burns in children are to cover the wound with sterile compresses and to quiet the pain of the child until he can be brought to a place where treatment can be given. The use of morphine in children under 5 years of age is contraindicated. The giving of blood and plasma transfusions is essential when burns are severe. Good results have been obtained with the use of a tannic acid salve.

HIGGINS, Boston.

Miscellaneous

THE USE OF THE SUPPOSITORY AS A VEHICLE IN SULFONAMIDE THERAPY. JAMES H. PARK JR., J. Pediat. **23**:326 (Sept.) 1943.

To avoid the gastric irritability due to oral administration of sulfonamide drugs, which interferes with the absorption of the drug and with the maintenance of the desired intake of fluids and food, the author suggests that the drug be prescribed in the form of a rectal suppository. The base employed in making the suppository is oil of Theobroma, which melts quickly in the rectum, leaving the drug available for reasonably rapid absorption. Any desired dose may be utilized; however, suppositories containing 7.7 grains and 15.4 grains of the preferred sulfonamide drug have been satisfactory in most instances. The rectal dose is twice that given by mouth.

Thirty minutes before treatment is instituted a cleansing enema of warm water should be given. The parent or nurse is instructed to then insert one suppository into the rectum, for retention, and to repeat this at

stated intervals. The buttocks should be held firmly together for fifteen to twenty minutes or strapped with adhesive plaster if necessary to prevent expulsion of the medicament. Estimations of the level of the sulfonamide drug in the blood have demonstrated that this method of treatment is as efficacious as that by mouth.

• FROM THE AUTHOR'S SUMMARY.

PROBLEMS IN SAFEGUARDING ADOPTIONS. HUGH K. BERKLEY, J. Pediat. **23**:344 (Sept.) 1943.

The first step in an adoption is the selection of a home where the potentialities of the child will be recognized and where he is likely to find emotional satisfaction. When an unrelated child is placed in a permanent home, professional skill is necessary to make sure that the persons selected as the future parents are those with whom the child is most likely to be happy and emotionally well adjusted. The safest procedure is to act through an agency with authority to accept guardianship. Acting through such an agency also assures the foster parents that the child taken into their home will not be removed unnecessarily. A frequently overlooked advantage of placement by an agency is the fact that the child has the benefit of a continuing interest in his welfare.

Because an adoption is a life plan, not just for babyhood, it is important to delay placement plans until the child is old enough so that his particular needs can be determined and the selection of a home and parents for him be made with these needs in mind. The Children's Bureau of the United States Department of Labor considers four months as the earliest advisable age for adoption.

The age of the child in relation to the ages of the foster parents must be carefully considered. They should have a life expectancy such as to assure that the child may reach maturity during their life time. They should be young enough to share the child's interests. It is also important that they shall not have adopted the child in anticipation of his supporting them as soon as he reaches maturity.

Satisfactory laws are not of themselves sufficient safeguards for adoptions unless supported by intelligent administration. Even without uniform laws considerable uniformity has been achieved by the acceptance of certain desirable safeguards. These include:

1. *A social study or investigation of every petition to adopt a child.* This is important, for the desire of a family for a child is not in itself sufficient evidence that it should be permitted to adopt a particular child, or perhaps even any child. Further, the mere availability of a child for adoption is not proof that the child is adoptable material.

2. *A report to the court after the social study.* A sound study loses much of its value unless the information obtained is presented to the court in such form that it will provide a basis for the final decision, which, of course, rests with the judge hearing the petition for adoption.

3. *A required period of residence for the child in the home before adoption becomes final.* A "period of absorption" allows the child and the foster parents to become adjusted to each other. Supervision and assistance to the prospective adoptive parents have great value in protecting the welfare of the child. An interlocutory period of one year with a supplementary report at the close of that period is recommended.

4. *A carefully drawn provision for consent that respects the rights of the natural parent.* Consent from a legally qualified authority should be required in every

adoption, parental rights having been terminated either by court action or by voluntary relinquishment. A second court action should be required to determine the merits of the proposed adoption so far as the welfare of the child is concerned.

5. *A plan for the protection of all official records of adoption from persons who have no legitimate reason to be permitted access to them.* It is advised that access to records of adoption be limited to "parties of the action." It is further advised that prior to "the action" parental rights be transferred to an agency. This obviates the possibility of the child's own parent or parents becoming "parties to the record" with the right to see the record of adoption.

6. *Restriction of jurisdiction in adoption to residents of the state and, except in exceptional circumstances, to residents of the county where the adoption is filed.* The lack of protection for records of adoption has probably influenced some prospective adoptive parents to file petitions for adoption in jurisdictions other than the one in which they reside. Such interstate traffic cannot fail to produce undesirable situations or abuses.

7. *A plan for a report of every adoption to the division of vital statistics in which proof of birth is included together with the date of the adoption and sufficient information about the foster parents to make possible the filing of a certificate of adoption in the new name of the child and in the names of the foster parents.* A provision requiring the filing of official reports of every adoption would make possible an accurate statistical count of the number of adoptions in each state as well as some additional information about the children adopted and the persons adopting them. A certificate of birth indicating the child's legal name, the date and place of his birth, the registration number of the original certificate of birth and the date it was filed is recommended. This presents proof of birth and citizenship, does not indicate either adoption or birth out of wedlock, and spares the child any possible future embarrassment because of the circumstances of his birth.

Legislative safeguards in adoptions are important but must be strengthened by administrative practices so that the intent of the laws may be actually realized. Many good laws never serve their purpose because of the lack of provisions for their administration.

SHMIGELSKY, Chicago.

PULMONARY MANIFESTATIONS FOLLOWING INGESTION OF KEROSENE. LEONARD I. LESSER, H. STEPHEN WEENS and JOHN D. McKEV, J. Pediat. **23**:352 (Sept.) 1943.

Accidental ingestion of kerosene by young children is not uncommon. During a two year period 33 patients from 1 to 3 years of age were studied at Grady Hospital. Most of the patients had fever, the temperature ranging from 99 to 104.5 F. Vomiting and coughing were frequently observed. Ten patients were drowsy and 2 patients were comatose on admission to the hospital. Though clinical signs of pneumonia were present in only 8 of the 33 patients, pulmonary changes were demonstrated roentgenologically in 77 per cent of the patients examined. Pulmonary edema, hemorrhage and superimposed inflammation were observed in one autopsy and in animal experiments. Roentgenologically these pulmonary changes appear as mottled, confluent or nonconfluent densities in the lungs, and they may be demonstrated within a few hours after the ingestion of kerosene and may disappear after an interval of several days. In animal experiments it was demonstrated that the pulmonary changes are brought about by aspiration

of kerosene into the respiratory tract and are not the result of absorption from the gastrointestinal tract with subsequent excretion into the lungs.

SHMIGELSKY, Chicago.

INFLUENCE OF VARIOUS DRUGS ON THE THRESHOLD FOR ELECTRICAL CONVULSIONS. M. L. TAINTER and others, *J. Pharmacol. & Exper. Therap.* **79:42** (Sept.) 1943.

Using a special electric device the authors determined the convulsive threshold of unanesthetized rabbits. As a group the depressant drugs raised the convulsive threshold while the excitant drugs (strychnine, nikethamide and others) were irregular in action; only picrotoxin, even in small doses, lowered the threshold to a considerable degree. Thyroxin lowered the threshold to epileptiform convulsions more than any of the other agents tested, the threshold being reduced from an average of 23.1 milliamperes in the control period to 15.7 milliamperes after nineteen days of thyroxin medication. This reduction suggests a possible physiologic basis for the impaired neuromuscular control and the poor poise of clinical hyperthyroidism. Many other drugs were tested also, with which the results were less striking.

PILCHER, Cleveland.

BLOOD LEVELS OF SULFADIAZINE, SULFAMERAZINE AND SULFAMETHAZINE IN RELATION TO BINDING IN THE PLASMA. D. ROURKE GILLIGAN, *J. Pharmacol. & Exper. Therap.* **79:320** (Dec.) 1943.

Working with human blood in vitro the authors found that sulfamerazine, sulfamethazine and their acetyl derivatives were bound in plasma to a much greater degree than is sulfadiazine. From available evidence it is probable that the same relation holds true in vivo.

The relative extent of binding of these drugs in the plasma is discussed with respect to the interpretation of rates of absorption from the rate of increase of the concentration of the drugs in the blood and with respect to its possible bearing on the relative therapeutic effectiveness of a given blood level of the different drugs.

PILCHER, Cleveland.

ROLE OF INOSITOL IN ALOPECIA OF RATS FED SULFASUXIDINE. EDWARD NIELSEN and A. BLACK, *Proc. Soc. Exper. Biol. & Med.* **55:14** (Jan.) 1944.

Inositol, 5 mg. six days weekly, succeeded in curing rats of alopecia produced by the administration of sulfasuxidine in addition to a synthetic diet believed to be complete nutritionally. From the beginning of the time inositol was incorporated in the diet the growth was better, and the fur coat was smooth, with normal luster.

HANSEN, Galveston, Texas.

STUDIES ON GUINEA PIGS AFTER REPEATED ADMINISTRATION OF PARALDEHYDE. EMMETT B. CARMICHAEL, F. A. KAY and G. W. PHILLIPS, *Proc. Soc. Exper. Biol. & Med.* **55:22** (Jan.) 1944.

Paraldehyde was injected intraperitoneally into adult male guinea pigs three times a week for four weeks. The average weight dropped from 499 to 469 Gm.; the length of time from the injection until the onset of sleep increased from eighty-five to one hundred and twenty seconds; the duration of sleep dropped from ninety-five to thirty-one minutes and the length of hypnosis dropped from two hundred and thirty-one to one hundred and sixty-seven. These observations indicate that guinea pigs acquire a tolerance to this drug.

HANSEN, Galveston, Texas.

GALACTOSE POISONING IN CHICKS. HENRIK DAM, *Proc. Soc. Exper. Biol. & Med.* **55:57** (Jan.) 1944.

Incorporation of 54.6 per cent galactose in the diet of chicks within a few days caused them to be seized with spasms, and in several days they succumbed. Cataract did not develop in these chicks, as it did in rats fed galactose, but this may be due to the fact that the chicks died within such a short time that cataract did not have time to occur. Galactose fed at a 10 per cent level to chicks did not cause symptoms. The galactose in the blood was high, but the dextrose in the blood was about normal. Muscle glycogen was also normal, but liver glycogen was almost zero. The mechanism of this disorder is not clear to the author.

HANSEN, Galveston, Texas.

EXPERIMENTS ON THE TOXICITY OF THE CALCIUM SALT OF PENICILLIN. PAUL GYÖRGY and P. C. ELMES, *Proc. Soc. Exper. Biol. & Med.* **55:76** (Jan.) 1944.

Freeze-dried calcium salts of penicillin were found to be no more toxic to mice than the sodium salt of penicillin. The dose employed in some of these experiments was approximately fifty times as great in proportion to body weight as the daily dose of sodium salt used at present in human therapeutics. No toxic signs developed when the calcium salts were administered to a human subject. The authors conclude that satisfactorily purified calcium salt of penicillin is not more toxic to human beings or mice than its sodium salt.

HANSEN, Galveston, Texas.

PHEMERIDE: A NEW ANTISEPTIC DETERGENT. C. N. ILAND, *Lancet* **1:49** (Jan. 8) 1944.

Phemeride (paratertiaryoctylphenyldiethoxybenzyl-dimethyl ammonium chloride) probably acts as an antiseptic by disrupting or interfering with the functions of the bacterial cell membrane.

The material was obtained as a white powder without odor which dissolved readily in water and alcohol. A small series of clinical tests was made. Laboratory and clinical tests suggested that phemeride is inhibitory to the common pathogens in dilutions not toxic to the tissues.

LANGMANN, New York.

BODY TEMPERATURES IN SHOCK. R. D. WRIGHT and J. DEVINE, *M. J. Australia* **1:21** (Jan. 8) 1944.

In patients suffering from shock the average rectal (internal) temperature on admission to the hospital was 99.3 F. and the average oral temperature was 96.7 F. A drop in internal temperature is not usual in shock, but if the patient is subjected to low environmental temperature the internal temperature drops as readily as that of normal subjects in similar circumstances. The oral temperature is, however, frequently lower than that of normal persons. In some instances in which no heat was applied after admission to the hospital and the patient was merely covered with blankets, the rectal temperature rose well above normal limits. Practical considerations arising from these observations are the following: (1) Heat should not be applied to patients suffering from shock until the rectal temperature has been taken; (2) repeated observation of the rectal temperature of the patient after admission to the hospital will prevent deleterious overheating, and (3) heat should not be applied to a patient unless facilities are at hand to supplement the loss of circulating blood that occurs as a result of a change from peripheral vasoconstriction to vasodilatation.

GONCE, Madison, Wis.

Book Reviews

Feeding Babies and Their Families. By Helen Monsch and Marguerite K. Harper. Price, \$3.50. Pp. 386, with 74 illustrations, 51 numbered and many unnumbered tables. New York: John Wiley and Sons, Inc., 1943.

From years of experience in feeding mothers and children and in teaching family nutrition the authors have compiled a volume which will prove informative and stimulating to doctors, nutritionists, home economists and dietitians and will merit their recommending it to women interested in assuring their families every nutritional advantage possible. The book is a comprehensive summary of the best scientific information available concerning foods, their preparation and feeding, and their influence on the life of mother, and fetus, infant, child, adult and aged person. The text is informal, with humor and pathos intertwined to dramatize the essential role that foods have in building healthy bodies. The emphasis is placed on the practical problems of feeding rather than on academic considerations, and the presentation is unusual in its lack of dogmatism. Both sides of controversial issues are presented, and a great effort has been made to explain the "why" of each of the many phases of good nutrition.

Under chapter titles such as "Why Eat?", "The Baby is Coming" and "The Toddler Tattles" and subtitles equally light, the practical application of the most recent knowledge of nutrition is presented clearly. The material on food composition (calories, fats, proteins, minerals, vitamins, amino acids, iodine, fluorine) serves as the background for consideration of nutritional needs throughout life and how they best can be supplied. Diets are given for all ages, based on the daily allowances recommended by the National Research Council in 1942 and presented in terms of common foods and supplemented with quantitative weekly menus. The special advantages or disadvantages of individual foods are discussed, as well as possible substitutions and supplements to meet special conditions. A wealth of useful information not usually found in literature on feeding is presented under headings such as "Customs and Traditions," "Religious Beliefs," "Insufficient Breast Milk," "Eating Between Meals" and "Eating Outside the Home."

The authors state their hope "that the book will be valuable not only as a textbook for college students of family nutrition but also as a guide for intelligent mothers in bringing up their families." The latter objective is accomplished so well that its attainment could not avoid detracting from the book's usefulness in the classroom, though not from its value as a reading reference. The student, however, would miss detailed discussions of other environmental, physiologic and genetic factors. Also, organization of the material for a lay audience is not entirely compatible with the demands of classroom teaching; illustrations and tables are numbered separately within the chapters, and while the profusion of subject headings in the text is useful, it involves separation and repetition of some of the material. Only the authors cited and the headings are indexed; this provides adequate general reference but not complete contact with all the material within each section.

Under the title "We are Indisposed," the final chapter is devoted to discussion of some of the common ailments

of childhood and later life which are frequently caused by misfeeding. Sound, practical advice on prevention is reinforced by effective logic and the histories of pertinent cases. It is regrettable that the title "treatment" is used for the sections on dietary care of the child with colic, indigestion, constipation, diarrhea, enuresis, colds, allergy and eczema. Readers might infer that this treatment constituted all necessary care and obviated the need of any medical attention. This oversight on the part of the authors will be corrected, no doubt, in future printings. One other terminologic consideration is worthy of attention: the expression "symptoms of good nutrition" is a misnomer, since in good nutrition there can be only the *absence* of symptoms of malnutrition.

Supplemental information which should prove useful to the student of family nutrition as well as to the homemaker has been assembled in an appendix. Among the tables are abbreviations and equivalents of common, metric and avoirdupois measures; equivalent weights and volumes of foods, and the weights and "cup" capacities of standard sizes of tin cans. The list of daily allowances for specific nutrients recommended by the committee on foods and nutrition of the National Research Council is reproduced and its use simplified by the insertion of tables which show the nutritive values of average servings of common foods. From these tables the adequacy of the intake of food can be estimated with a minimum expenditure of time.

Medical Clinics on Bone Diseases: a Text and Atlas. By Dr. I. Snapper. Price, \$10.75. Pp. 225, with 30 plates. New York: Interscience Publishers, Inc., 1943.

This book gives an excellent account of a number of nonsurgical diseases of bone that have come to be better understood as a result of researches in endocrinology, biochemistry and nutrition during the past twenty years. Generalized osteitis fibrosa cystica (von Recklinghausen's disease) is discussed in relation to hyperparathyroidism, and a chapter is devoted to hyperplasia of the parathyroids secondary to other diseases of bone. Fetal, infantile and late rickets and osteomalacia are discussed in relation to avitaminosis D. There are also clinics on osteitis deformans (Paget's disease of the bone), lipid granulomatosis of bone, Gaucher's disease, and multiple myeloma. In the discussion of each condition, a few cases are reported in great detail with extensive biochemical, roentgenographic and histologic studies, with the result that a vivid picture is presented. The book is particularly helpful from the standpoint of diagnosis, but it also throws considerable light on the treatment of those diseases of bone which are related to the parathyroid and to nutrition.

Jornada pediátrica de la Habana. Edited by M. V. Fresneda. Price, \$5.00. Pp. 538, with 122 illustrations. Habana, Cuba: Sociedad Cubana de Pediatría, 1942.

The transactions of the Cuban Pediatric Society for the meetings of Dec. 12 to 15, 1940 open with a twenty-three page résumé by Professor Inclan of the history of pediatrics in Cuba. This is followed by thirty-five articles on various pediatric subjects by the members

of the society. The articles are well printed and profusely illustrated with charts, tables and roentgenographic prints.

As the Child Grows. By Helen Brenton Pryor, M.D. Price, \$3. Pp. 400, with 16 diagrams and 8 charts. Chicago: Silver Burdett & Company, 1943.

The preface, written by Professor Hanna of Stanford University, states the case perfectly when it says that "the purpose of this book is to help teachers, parents and all others who guide youth to gain a clearer insight into the needs of children by understanding better the distinctive characteristics of boys and girls in the various stages of their growth and maturation. It attempts to picture the child as a whole."

To marshal all of the facts and opinions necessary to accomplish this appalling task requires a courageous person; Dr. Helen Pryor has made the attempt, in general with good results. I believe that the preface is substantially correct when it states that "this volume will find a wide reception among teachers and parents because it develops the scientific bases of these differences in a language and style that the layman to medicine and physiology can understand, and because it gives many practical suggestions to parents and teachers for handling the problems peculiar to the child at each stage of its development."

However, the "layman to medicine and physiology" will have to concentrate, and sharply, for the mass of factual material is tremendous. I question whether many teachers of children, much less parents, have the scientific background and surplus intellectual energy to digest such material as is presented on embryology and genetics. Medical students in the preclinical years would no doubt be deeply grateful for such condensation and popularization of weighty material.

The pediatrician will be grateful to find between the covers of one book so many of the opinions held by social workers, psychologists, geneticists and persons of almost every other type concerned with children, whether he agrees with them or not. He probably will object to the classification of all human beings, even roughly, into "broad-built lateral types" and "slender-built linear types," for metamorphosis is certainly observed at various levels of growth. He will wonder if it is really established that "at the critical moment during the second month of gestation the mother may run a high fever and halt the growth of the thyroid gland, causing so-called Mongolian idiocy. This is the sort of thing that should be more widely known" (if true). He will reject as unproved the statement, in the discussion of poliomyelitis, that "large doses of convalescent serum are helpful in reducing the severity of the attack." The inclusion of this and other definite statements of opinions on medical issues which are still most controversial and of opinions quite contrary to leading pediatric opinion, leads one to hope that the same license is not being taken in fields with which the pediatrician is less familiar.

There is a comprehensive, well chosen bibliography which is attractively and accessibly arranged. The appendix contains material on such diverse subjects as adolescent development in girls, assessment of growth, determining of body build, studies of basal metabolism and of diseases and overweight and underweight children.

From what has been said previously it becomes apparent that almost everything that concerns life before maturity is discussed, and in a readable manner. Considering the material, I expect to use the book for quick,

easy reference on certain constants in pediatrics, for its bibliography on fields related to pediatrics and for its summary exposition of these related fields.

The Arthropathies: A Handbook of Roentgen Diagnosis. By Alfred A. de Lorimier. Price, \$5.50. Pp. 319, with 678 illustrations. Chicago: The Year-book Publishers, Inc., 1943.

It is a joy to read and use this handbook by Colonel de Lorimier, Commandant of the Army School of Roentgenology, Memphis, Tenn. Every pediatrician, internist, surgeon and roentgenologist should welcome it as a valuable *vade mecum*. The author's introduction states that an evaluation of the roentgen evidence concerned with conditions in and about joints is dependent on four points, a knowledge of embryology, a knowledge of detailed anatomic relations, an understanding of pathologic changes and familiarity with the clinical aspects of the particular case, including laboratory data. A description of normal joints and points of roentgenologic interest and importance based on their anatomy introduces the discussion. The arthropathies are then described, using a classification based on the etiology so far as known.

Part I deals with the peripheral joints explaining by clearly marked illustrations the developmental malformations and pathologic changes. The osteochondropathies, specific and nonspecific, of juvenile and adult types, are discussed next, followed in order by the arthropathies in which the changes are essentially concerned with mechanical stresses, those related to protein reactions, toxins or bacterial invasion, the true arthritides and lastly gout, neoplasms and various miscellaneous disorders such as calcification of the medial collateral ligament of the knee due to trauma (Stieda-Pellegrini disease), *ainhum* and *scleroderma*.

Part II deals with the joints of the spine including developmental formations, osteochondropathies, osteoarthropathies, neuroarthropathies, toxic arthropathies, infections, arthritis, neoplasms and miscellaneous disorders from *fragilitas ossium* (osteogenesis imperfecta) and hyperparathyroidism to regional tumors and aneurysms.

The small compact format of the book lends to its attractiveness. The reader may find a magnifying glass of great assistance in reading the film reproductions. The only possible criticism of the whole volume may be that the legends for the illustrations are printed in type which is too small.

Kinderzeichnungen in vergleichend psychologischer Beleuchtung: Untersuchungen an serbischen Kindern. By Franziska Baumgarten, Ph.D., and M. Tramer, M.D. Price, 3.50 Swiss francs. Pp. 210, with 57 figures. Basel, Switzerland: Benno Schwabe & Co., 1943.

The authors report the results of psychologic studies of 272 Serbian children 5 to 12 years old who were sent to camps in Switzerland for recreation. Because of difficulties in language, the psychologic tests were based on three types of drawings. The children were asked to draw (1) the picture of a person, (2) a subject left to the imagination of the child and (3) a subject referring to their homeland.

It is instructive to a pediatrician to see how many interesting conclusions can be reached by using children's drawings for psychologic tests. The boys up to the age of 9 years always drew pictures of boys, never of girls; with increasing age the percentage of girls in the pictures increased and at the age of 12 years only

70 per cent drew pictures of boys. Similar observations were made on Swiss children. The authors offer as an explanation that younger children prefer playmates of the same sex but that this desire diminishes with approaching puberty. The majority of the children selected as the subject of free choice a house or something referring to the home. The drawings of the boys were exact and positive and demonstrated a sense of objectivity, while the drawings of the girls were guided mostly by sentimentality. The book includes many other interesting conclusions and discussions.

The fifty-seven figures given as examples of the children's drawings are admirably reproduced, printed on an excellent type of paper.

White Blood Cell Differential Tables. By Theodore R. Waugh, Pathologist in Chief, Royal Victoria Hospital; Associate Professor of Pathology, McGill University, Montreal, Canada. Price not given. Pp. 15, with 10 tables. New York: D. Appleton-Century Company, 1943.

There has been an increasing conviction in recent years among clinicians and laboratory workers that the finer diagnostic value of the differential leukocyte count resides in the absolute rather than the relative number of each type of cell present. Consequently many laboratories now report the differential count in terms of the actual number of polymorphonuclear leukocytes, lymphocytes, monocytes and eosinophils, instead of in the traditional percentage figures. This information is of particular significance in cases of illness in infants and children and in cases of leukopenia and leukocytosis. Ordinarily the absolute value for each type of cell may be obtained from the conventional differential count by calculation of the given percentage of the total count. This procedure is time consuming when large numbers of counts are done, and to obviate this the author has prepared a set of convenient tables. Besides providing the reader with tables for rapidly computing the actual number per cubic millimeter of each type of white cell from the known differential percentage, the author has included some concise introductory notes on white blood cells and differential counting for the novice. The use of the tables is clearly set forth and specific examples are given. These convenient tables should be welcomed by clinicians specifically interested in interpreting hemograms. Their value and convenience are self evident to pathologist, hematologist and laboratory technician.

Physique, Personality and Scholarship: A Co-operative Study of School Children. Monograph of the Society for Research in Child Development, vol. 8, ser. 34, no. 1. By R. Nevitt Sanford, Margaret M. Adkins, E. Bretney Miller, Elizabeth A. Cobb, and others. Price, \$2. Pp. 705. Washington, D. C.: National Research Council, 1943.

This study, for the major part of which the senior author is responsible, covers the developmental history of the school child and includes detailed data on 48 children aged 5 to 14 years. The approach is an intensive one, using biologic, psychologic and other technics to study children not as discrete organisms but as living, changing, functioning human beings at one of the most important stages of their development.

The investigators have taken the point of view that no single factor is, by itself, of sufficient significance to merit full consideration unless other related aspects of development are included in the evaluation. This monograph, therefore, is concerned not only with the several physical, psychologic, physiologic and sociologic vari-

ables but, more closely, with their many interrelationships and the effects on personality, adjustment and school success thus produced. The circumstantial histories of cases and the precise descriptions of traits add interest and individuality to the volume.

Safe Convoy: The Expectant Mother's Handbook.

By William J. Carrington, M.D. Price, \$2.50. Pp. 256, with no illustrations. Philadelphia: J. B. Lippincott, 1944.

This book is an addition to the handbooks for expectant mothers, of which there already are a number. It differs somewhat from most of those which have already been published in that it contains also a considerable amount of information concerning the care of babies. The book is written in an attractive style, and historical allusions are interpolated here and there, which add to the interest of the story which is being told.

Reproductive anatomy is explained briefly and well. A considerable amount of attention is given to diet; the vitamins are dealt with simply and adequately. The dietary section is to be commended, although the reviewer had supposed that Prochownik's diet for the production of a small child had been relegated to the limbo of forgotten things. The chapters on diagnosis and on labor are well done and will be understood easily by the average mother-to-be.

The latter part of the book reaches over into the domain of pediatrics, with a section on the care of infants, including some pages dealing with common disorders of infants.

A feature which seems new is the short chapter devoted to that usually neglected person the father of the infant, entitled "Fathercraft."

The book may be commended as a simple and accurate guide for expectant mothers.

Pathology and Therapy of Rheumatic Fever. By Leopold Lichtwitz, M.D., lately Chief of the Medical Division of the Montefiore Hospital, and Clinical Professor of Medicine, Columbia University. Foreword by William J. Maloney, M.D. Edited by William Chester, M.D. Price, \$4.75. Pp. 225, with 69 illustrations. New York: Grune & Stratton, Inc., 1943.

This book arrives on the scene when rheumatic fever has become a public health problem of growing importance in both civil and military life. Dr. Lichtwitz dwells particularly on the pathology and therapy of the disease. He has made an exhaustive study of the literature, and the bibliography at the end of each chapter is extensive.

The author argues that rheumatic fever is a manifestation of allergy, and his thesis is summed up in the following quotation: "The pathologic basis of this disease is the allergic sensitization of certain mesenchymatous tissues." He contends that the disease is one of defense, not of invasion, and that it has its counterpart in serum sickness. Lack of defense is termed anergy and its excess hyperergy. The mechanism of hyperergy is dependent on the allergic sensitization of the person, which, in turn, is influenced by antigens of bacterial origin. The author recognizes the hemolytic streptococci as probable inciting bacterial agents and builds up from this his theory of allergic response.

There is much in the book which holds little interest for the pediatrician, but, on the other hand, there is much of value, particularly to those who are interested in the clinical manifestations, pathology and therapy of rheumatic fever and rheumatic heart disease. Lastly,

the foreword is well done and is recommended for careful reading.

Orthopedic Nursing. By R. N. Funsten and Carmelita Calderwood. Price, \$3.75. Pp. 559, with 181 illustrations. St. Louis: C. V. Mosby Company, 1943.

The great importance of competent, experienced nursing for orthopedic patients is appreciated by all who are responsible for the end results. This is particularly apparent now, when the turnover in the nursing personnel is apt to be higher than ever before.

This book will be a great help in the teaching of the principles of orthopedic nursing.

Attention to detail makes the difference between good and bad technic, and this is especially true in the care of orthopedic patients. It is impossible to give in detail the various technics used throughout the country, but the basic procedures are described. Each orthopedist will want certain changes made to suit his own methods of handling the different types of orthopedic conditions.

Office Treatment of the Nose, Throat and Ear.

By A. R. Hollender. Price, \$5. Pp. 480, with 33 illustrations. Chicago: The Year Book Publishers, Inc., 1943.

This book fills a much needed place in the field of otorhinolaryngology. To the intern or hospital resident called on to treat transient ambulatory patients in the absence of the attending surgeon and to the man on whose shoulders the practice of the specialty has been forced by the fortunes or misfortunes of war the book is invaluable. It is well illustrated, clearly written and concise. In each chapter the author has discussed the various methods in vogue at the present time in the treatment of specific disorders, and at the end of the chapter he has summarized the discussion and evaluated the methods from his own experience.

The work is complete and thoroughly modern.

Pioneers of Pediatrics (Historia medicinae, Volume 9). Edited by Dr. Abraham Levinson. Second edition. Price, \$2. Pp. 119, with 29 illustrations. New York: Froben Press, Inc., 1943.

This is the second edition of a book which contains short reviews of the works of various pediatricians down the ages. It is instructive, especially in the first few chapters, which deal with other than contemporaries. Not every one will agree with the choice of men or the distribution of emphasis, since this, of course, is a matter of the personal equation. On the whole, the book is one which claims interest and deserves commendation.

Doctor Colwell's Daily Log for Physicians, 1944.

Price, \$6. Champaign, Ill.: Colwell Publishing Company, 1943.

This book for 1944 is a replica of those for previous years but also contains a new form for nonprofessional deductions and a tax table or schedule furnished by the Treasury Department. These additions should prove useful.

Baby Doctor. By Isaac A. Abt. Price, \$2.50. Pp. 310, with no illustrations. New York: McGraw-Hill Book Company, Inc., 1944.

When Dr. Abt finished his premedical work at Johns Hopkins University, he appealed to Professor Welch for advice as to the best medical school to go to. The

Johns Hopkins Medical School was not started until five years later. Dr. Welch assured him that no medical school of that day was "too good" and added: "It won't make any difference where you go. Everything depends on you." That he spoke wisely then, as always, is demonstrated in this little book.

As compared with modern standards of medical education, the medical schools of that day were "none too good." Most of them still had only an ungraded course of two terms of six months each, but the old Chicago Medical College, a department of Northwestern University, offered a graded course of three terms of nine months each, the first medical school to do so in this country, and it was in Dr. Abt's home town. So he entered that school and graduated with the famous class of 1891. That things weren't any too good even in the Chicago Medical College is shown, for example, in two statements: "There were only three full time paid employees, a janitor, a registrar and the professor of chemistry"; and the dean of the school "did not believe in bacteriology, asserting that it was only a passing fad," although it was seven years since Koch had published his epochal work on the tubercle bacillus. After eighteen months of internship at the old Michael Reese Hospital and another eighteen months in Vienna, Berlin and London, the young doctor hung out his shingle in Chicago and soon demonstrated that Professor Welch's second statement was well founded.

There were only a few men in the whole country at this time who restricted their work to pediatrics; nearly all of the men who were especially interested in work with children did some "bread and butter" general practice. Dr. Abt followed the same course, and, having had some training in obstetrics while abroad, he ushered a few babies into the world and so increased his pediatric practice. He also rectified a poor job of surgery on the tail of a dog that was to be entered in a dog show, set some bones and stitched up some cuts for another one and did an autopsy on a canary after having failed to cure it; he found peritonitis. Soon, by a process of elimination, he was able to restrict his work to children; his aim from the start in spite of the warnings of all his colleagues. Work in clinics, hospitals and laboratories and at a couple of municipal jobs added to his practice, kept him fully occupied and on his toes. If genius is measured by a man's ability to work, as some one said, Dr. Abt has a claim to that title. He was, and still is, an indefatigable worker.

Dr. Abt's career in pediatrics and the development of that specialty ran a nearly parallel course from the beginning and for well over fifty years. They grew up together, and each helped the other. It is this that adds significance to the book, giving it a twofold interest and purpose. On the one hand, it is the autobiography, the intimate personal narrative of the trials as well as the rewards, of a physician whose life was devoted to the care of children in the widest sense, both as a pioneer in and as one of the foremost exponents of pediatrics in this country. On the other hand, it traces the development of pediatrics from its infancy, step by step, as new procedures and discoveries changed its course, up to its present full maturity, as Dr. Abt himself lived through and helped in the development.

The book is written clearly and simply, as are all good books, and the layman need have no fear that it is beyond his depth. Nearly every step in the progress of care of children is illustrated by an anecdote, the story of a case or of a medical or social situation, and

through it all runs an irrepressible and genial humor and a refreshingly human interest that never forgets the child himself.

To physicians of only a little later vintage the book has an especial appeal; to younger physicians it should be both interesting and stimulating. Laymen, the parents, will find the book interesting and informative, both because it portrays a long and outstanding professional career and because it will make them realize why their children can now be so well guarded and cared for. This is a "doctor book" that ought to have a wide field of human interest and usefulness.

The War and Mental Health in England. By James M. Mackintosh, M.D. Price, 85 cents. Pp. 91, with no illustrations. New York: The Commonwealth Fund, 1944.

Dr. Mackintosh is professor of preventive medicine at the University of Glasgow. He has long been interested in mental health and has identified himself with the groups which are doing work in that field. Part I deals with the impact of war; part II, with mobilization for peace.

During the "process of adjustment" (1939-1940) there was an increase in mental stress due to mobilization and evacuation. Rapid social changes, stress brought about by uncertainties, breaking up of homes, placing of men in new positions to which many could not adjust, increased strain from long hours, unhealthy conditions brought on by blackouts, lack of recreation, shortage of food and favoritism brought on a sharp increase in severe attacks of illness, notably of rheumatism and ulcers. The anxiety of adults was passed on to children. Evacuation, though efficiently done except that human elements were omitted, was harmful to the minds of children. There was a letdown in discipline; children suffered from being placed with persons of different social classes. Easing of anxiety followed the confirmation that "Now we are at it," and much has been done to overcome the mental stresses that were at first overlooked.

The fall of France was so rapid that progressive mental adjustment was out of the question. Churchill's speeches (1940-1941) and the evacuation of Dunkirk restored the national balance of mind, and the battle of Britain brought back the full measure of public confidence. The people of Great Britain and the United States have a mental advantage in that they feel they cannot be defeated.

In 1941 and 1942 the attack on Russia gave the British an opportunity to enter the offensive phase of the war and to plan for the future. These changes greatly improved their mental health as did an improved system for distribution of food.

In 1943 the mental attitude of the English people improved rapidly with the victories at Stalingrad and in Egypt. By this time children in England were permanently placed for the duration. The effects of the placement on the adjustments to be made at the end of the war are discussed.

Psychiatric hospitals and facilities for child guidance are increasing, and the rehabilitation of children and adults after the war is receiving special consideration. Both governmental and volunteer organizations are engaged in this work. The author points out the need for further teaching of psychiatry in medical schools.

This book contains a large amount of extremely interesting and valuable information on the effect of war on mental health and on the conditions that affect mental health, only a small percentage of which can

be introduced in a review. It should provide equally profitable reading for professional and for nonprofessional persons.

Functional Disorders of the Foot. By Frank D. Dickson, M.D., and Rex L. Diveley, M.D. Second edition. Price, \$5.00. Pp. 352, with 202 illustrations. Philadelphia: J. B. Lippincott Company, 1944.

This is a highly practical treatise on a subject which should be of great interest to the pediatrician and to the general practitioner as well as to the orthopedic surgeon.

It is unfortunate that the medical profession as a whole has not recognized the great amount of disability and discomfort produced by functional and anatomic disorders of the foot and has failed, therefore, to give these conditions the serious study and attention they deserve. Symptom-producing conditions of the foot constitute a real economic as well as a medical problem.

The chapters on the evolutionary development of the foot, on anatomy and physiology and on the primary causes of imbalance of the foot are elementary, but they represent fundamental knowledge which must be assimilated before accurate diagnosis and adequate treatment are possible.

The authors point out, correctly, that the early recognition and treatment of functional imbalance of the foot in early childhood, when the bones of the feet are in the process of calcification and growth, may result in an anatomic and physiologic cure. In the adult, however, such is usually not the case, and treatment is palliative and designed to relieve symptoms only. The pediatrician, therefore, is probably in a position to do more for the prevention of foot trouble than any one else in the medical profession.

The discussion of the McElvenny and Betts surgical procedure in the treatment of metatarsalgia is most interesting. I am sure that this operation will have a definite place.

The chapter on foot apparel is good, although there is undoubtedly room for a difference of opinion as to some of the characteristics of a "good" shoe.

The book is provided with drawings of methods of foot and ankle strapping and with pictures illustrating foot exercises.

Soviet Health Care in Peace and War. By Rose Maurer. Price, 10 cents. Pp. 48, with 5 illustrations. New York: American Russian Institute, 1943.

The author speaks from first hand contact with the medical institutions and practices of Soviet Russia, and since leaving that country she has kept in close touch with medical progress through reports and other literature. The first part of the book describes the health administration in times of peace and the second part the adaptation to the needs of war. The government holds itself directly responsible for the provision of health facilities and education in matters of health. The citizen is held responsible for availing himself of these opportunities. Protection of health at the place of work is facilitated through the cooperation of the trade unions. District health centers are numerous, and special provisions are made for the care of women and children and for rural medical facilities. Medical education is free, and the majority of students receive also an allowance for expenses. In return, graduates are expected to practice for five years in the locality in which the Health Commissariat decides their services are most needed. At the beginning of the war there

was a reduction in the medical curriculum, but this has been found inadvisable; now the full five year course is again operative. The splendid cooperation between civilian, military forces and medical workers is shown to be a large factor in the remarkable record of achievement in health. Individual responsibility for the welfare of all seems to be the motivating spirit. Before the war Soviet Russia had experienced a 40 per cent reduction in death rate in comparison with tsarist Russia. The death rates in Moscow and Leningrad were lower than those in Berlin, London or Paris. The lack of epidemics since the beginning of the war speaks for the health and the health organization of the civilian population and of the army. It is said also that the red army and air forces are virtually free from venereal disease.

Elements of Medical Mycology. By Jacob Hyams Swartz, M.D. Price, \$4.50. Pp. 190, with 80 illustrations. New York: Grune & Stratton, Inc., 1943.

This is an excellent small book which fulfils its avowed purpose as stated in the preface, "to serve the practitioner as a guide to the study of fungus diseases." It is also admirably suited to the student and to the practitioner who does not profess to be a mycologist. It is not at all an encyclopedic reference, and to the experienced mycologist it is only a primer.

The great merit of the book is its conciseness and simplicity. Outlines are excellent. Terminology is clarified and simplified and so illustrated as to eliminate much of the confusion that confronts the student or practitioner to whom fungous diseases are of only part time interest.

The clinical descriptions are a bit too brief, but the details are of course available elsewhere. The illustrations of clinical features of the diseases are too few and not particularly good; however, both the photographs and the drawings of direct preparations are most adequate. The information to be obtained from such simple procedures is given major space, as against the more difficult and highly specialized cultural studies. This emphasis is gratifying to the practitioner who lacks the facilities for complicated cultural studies.

Therapy, which is so important to the practitioner, is well covered in detail. Evaluation of questionable modalities is especially sane and helpful. This as well as other phases is up-to-date and is no mere rehash of other published works. The closing chapter is entitled "Sulfanilamide and its Derivatives: Effect on Fungi."

The glossary of terms encountered in mycology is adequate and helpful. The indexing is good. The outlines, both in the text and in the appended chart, are excellent both for teaching and for ready understanding of the field.

Psychology of Women. Volume I. By Helene Deutsch, M.D. Price, \$4.50. Pp. 399. New York: Grune & Stratton, Inc., 1944.

The author of this book has devoted many years to the study of feminine psychology. In this volume she presents a systematic study of the development of the personality of woman, using her own observations and those of other writers. Since over 200 pages is devoted to adolescence and the preceding years, it is of special interest to pediatricians.

Chapters devoted to prepuberty, early puberty, puberty, adolescence and menstruation are followed by chapters on the mature personality of women. The author care-

fully describes the instinctive and environmental factors which consciously and unconsciously influence the minds of girls and women and considers the large number of conflicting emotional problems which enter their minds. Normal growth and development are described, and the causes of mental ill health are discussed at length. Throughout the book the author emphasizes the fact that there are many emotional problems, usually conflicting ones, in the mind of every girl. If those problems become too complex and she cannot solve them, neuroses and other forms of mental ill health develop; these conditions can often be remedied by psychiatric treatment.

The author is a psychoanalyst and follows the Freudian approach to behavior. Her work has been largely with adults, but she has treated a great many girls. Although she has not worked directly with infants and children, except in "working back" with her patients, she has grasped and described the attitudes of parents which influence children.

The book is detailed, and well written and reveals a rare insight into the emotional development of women. It should be very helpful to pediatricians, even though the psychiatric nomenclature may make parts of the book rather difficult reading.

Something New About Health and Healing. By P. F. Van Den Daele, B.S. Price, \$3.00. Pp. 288. Boston: The Christopher Publishing House, 1944.

This collection of essays and notes is a unique combination of misinformation and much honest intent. The author is a bloodless surgeon, relying for diagnosis on the history and palpation and for treatment chiefly on manipulation and application of heat when the local temperature is low and of cold when the local temperature is elevated. He denies that germs can cause disease, deplores the use of serums and vaccines and explains the processes of disease as due to short-circuiting of nervous impulses.

In spite of these misconceptions, much of the advice about the nursing care of the patient and about diet is sound. Also his criticism of the too common practice of using drugs to overcome symptoms instead of searching for the underlying cause is not amiss.

News and Comment

PERSONAL NEWS

Promotion for Col. James G. Hughes.—Col. James G. Hughes, Medical Corps, Army of the United States, formerly of Memphis, Tenn., at 34 years of age has been promoted from lieutenant-colonel, becoming one of the youngest Medical Corps colonels in the Italian theater.

New Appointment for Dr. R. R. Struthers.—Dr. R. R. Struthers, professor of pediatrics at McGill University, Montreal, Canada, and physician-in-chief at the Children's Memorial Hospital, has accepted a position as pediatric consultant with the United Nations Reconstruction and Rehabilitation Administration. Dr. Alton Goldbloom has been appointed chairman of the department of pediatrics and acting physician-in-chief to the Children's Memorial Hospital.

Directory of Pediatric Societies *

INTERNATIONAL

INTERNATIONAL ASSOCIATION OF PREVENTIVE PEDIATRICS

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

INTERNATIONAL CONGRESS OF PEDIATRICS

President: Dr. Henry F. Helmholtz, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Charles F. McKhann, University Hospital, Ann Arbor, Mich.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston. Time: Postponed indefinitely.

INTERNATIONAL CONGRESS FOR THE PROTECTION OF INFANCY

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

ARGENTINE PEDIATRIC SOCIETY OF BUENOS AIRES

President: Dr. Martín Ramón Arana, 1809 Rodríguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguía, Cerrito 1179, Buenos Aires.

ASSOCIAÇÃO PAULISTA DE MEDICINA, SECTION ON PEDIATRICS

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Paulo de Barros Franca, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.

BRITISH PAEDIATRIC ASSOCIATION

President: Prof. L. G. Parsons, 58 Calthorpe Rd., Five Ways, Birmingham.
Secretary: Dr. Donald Paterson, 27 Devonshire Pl., London, W. 1.

DANISH PEDIATRIC SOCIETY

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjörup, Dronning Louises Børnehospital, Copenhagen.

NEDERLANDISCHE VEREENIGING VOOR KINDER- GENEESKUNDE

President: Dr. J. H. G. Carstens, Servaasbolwerk 14*, Utrecht.
Secretary: Dr. R. P. van de Kastele, Laan van Poot 340, 's Gravenhage.
Place: Different places. Time: Three times a year.

PAEDIATRICKÝ SPOLOK NA SLOVENSKU

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialkstr., Tel Aviv.
Secretary: Dr. A. Brün, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Angel A. Aballí Arellano, 17 No. 609 Vedado, Habana.
Secretary: Dr. Julio G. Cabrera Calderin, Hospital Mercedes L y 21 (Vedado), Box 2430, Habana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Fernando López Clares, 12/a. Medellín 191, Mexico.
Secretary: Dr. Jesus Gómez Pagola, Versalles 64, Mexico.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. E. Santos Mendoza.
Secretary: Dr. P. Oropeza, Hospital de Niños, Caracas.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Jose Alberto Praderi, Eduardo Acevedo 1132, Montevideo.
Secretary: Dr. Alfredo Ramon Guerra, Paysandú 824, Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.
Place: New York. Time: June 11-15, 1945.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Franklin P. Gengenbach, 1850 Gilpin St., Denver, Colo.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S
HOSPITAL SECTION

Chairman: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly, Mass.

AMERICAN PEDIATRIC SOCIETY

President: Dr. James L. Gamble, 300 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES
OF CHILDREN

President: Dr. R. R. Struthers, 906 Drummond Medical Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Edward M. Bridge, 219 Bryant St., Buffalo, N. Y.
Secretary: Dr. Mitchell L. Rubin, 1740 Bainbridge St., Philadelphia 46.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Eugene Smith, 385-24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Warren R. Sisson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. C. G. Ashley, 833 S. W. 11th Ave., Portland, Ore.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. Arild E. Hansen, University of Minnesota, Minneapolis.
Secretary-Treasurer: Dr. Albert V. Stoesser, 205 W. University Hospital, Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver.

SOUTHERN MEDICAL ASSOCIATION, SECTION
OF PEDIATRICS

Chairman: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.
Secretary: Dr. Angus McBryde, 604 W. Chapel Hill St., Durham, N. C.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Amas Gipson, 948 Forrest Ave., Gadsden.
Secretary-Treasurer: Dr. Ruth Berrey, 2021-6th Ave. N., Birmingham.

ARIZONA PEDIATRIC SOCIETY

President: Dr. Vivian Tappan, San Clemente, Tucson.
Secretary: Dr. Hilda Kroeger, Arizona State Health Dept. (Maternal and Child Welfare Division), Phoenix.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION
ON PEDIATRICS

Chairman: Dr. William C. Deamer, University of California Hospital, San Francisco.
Secretary: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Ludo Von Meysenbug, Box 3356, Daytona Beach.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. T. F. Davenport, 104 Ponce de Leon Ave. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB
OF CONNECTICUT

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Time: Three meetings a year.

ILLINOIS STATE MEDICAL SOCIETY, SECTION
ON PEDIATRICS

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Mark L. Floyd, Children's Hospital, Iowa City.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION
ON PEDIATRICS

Chairman: Dr. A. Clement Silverman, 603 E. Genesee St., Syracuse.
Secretary: Dr. Albert G. Davis, 307 Gas and Electric Bldg., Utica.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA,
PEDIATRIC SECTION

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

MICHIGAN STATE MEDICAL SOCIETY,
PEDIATRIC SECTION

Chairman: Dr. Charles F. McKhann, University Hospital, Ann Arbor.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. E. W. Hancock, 820 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. John M. Thomas, 1102 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Arthur H. London, 1105 W. Main St., Durham.
Secretary: Dr. Jay M. Arena, 604 W. Chapel Hill St., Durham.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Ben H. Nicholson, 301 N. W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Lonita Boggs, 301 E. Coffee St., Greenville.
Secretary-Treasurer: Dr. Hilla Sheriff, Wade Hampton Office Bldg., Columbia.

TEXAS PEDIATRIC SOCIETY

President: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Edwin A. Harper, 301 Rivermont Ave., Lynchburg.
Secretary: Dr. Emily Gardner, 1100 W. Franklin St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY,
SECTION ON PEDIATRICS

President: Dr. Andrew Amick, 1021 Quarrier St., Charleston.
Secretary: Dr. A. A. Shawkey, Professional Bldg., Charleston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND
PEDIATRIC SECTION

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. I. B. Silber, 10465 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO,
SECTION OF PEDIATRICS

President: Dr. I. Nelles Silverthorne, 170 St. George St., Toronto, Canada
Secretary: Dr. G. P. Hamblin, 2333 Bloor St. W., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry J. Cohen, 1975 Walton Ave., New York.
Secretary: Dr. Walter Levy, 12 E. 88th St., New York
Place: Concourse Plaza Hotel, 161st St., and Grand Concourse. Time: Second Wednesday of each month except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Harry A. Naumer, 37-8th Ave., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Granada Hotel. Time: Fourth Wednesday of October, November, February, March and April.

BUFFALO PEDIATRIC SOCIETY

President: Dr. A. Wilmot Jacobsen, 187 Bryant St., Buffalo N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Edward J. Wynkoop, 501 James St., Syracuse.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Morley D. McNeal, 2 N. Sheridan Rd., Highland Park, Ill.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

CINCINNATI PEDIATRIC SOCIETY

Secretary: Dr. T. Selkirk, 3530 Reading Rd., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati.
Time: On call.
President: Dr. Lloyd K. Felter, 3144 Jefferson Ave., Cincinnati.

DALLAS PEDIATRIC SOCIETY

President: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas, Texas.
Secretary-Treasurer: Dr. Gladys J. Fashena, 4585 Belfort, Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. John J. Pollack, 650 Maccabees Bldg., Detroit, Mich.
Secretary: Dr. Philip J. Howard, 2799 W. Grand Blvd., Detroit, Mich.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRICS
SECTION (ATLANTA, GA.)

Chairman: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Secretary: Dr. Harry Lange, 478 Peachtree St., N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

HOUSTON PEDIATRIC SOCIETY

President: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: College Inn, Houston. Time: Fourth Monday of each month.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Edwin H. Schorer, 1103 Grand Ave., Kansas City.
Secretary: Dr. H. E. Petersen, Kirkpatrick Bldg., St. Joseph, Mo.
Place: Kansas City General Hospital. Time: On call.

LOS ANGELES COUNTY MEDICAL ASSOCIATION,
PEDIATRIC SECTION

President: Dr. Oscar Reiss, 2200 W. 3d St., Los Angeles.
Secretary-Treasurer: Dr. Elena Boder, 1830½ Lucille Ave., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND
THE ACADEMY OF MEDICINE OF BROOKLYN,
PEDIATRIC SECTION

President: Dr. Abraham M. Litvak, 1145 Eastern Parkway, Brooklyn.
Secretary: Dr. Harold Levy, 750 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month, October to April, inclusive.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC.,
SECTION ON PEDIATRICS

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA,
SECTION ON PEDIATRICS

President: Dr. Harry A. Spigel, 2647 Connecticut Ave., Washington, D. C.
Secretary-Treasurer: Dr. Perry W. Gard, 2520 Woodley Rd., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of every month.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. F. T. Mitchell, 376 S. Bellevue Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. John H. Reynolds, 1628 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. F. J. Mellencamp, 324 E. Wisconsin Ave., Milwaukee.
Place: Milwaukee Athletic Club. Time: Second Wednesday of each alternate month, beginning with February.

NEW YORK ACADEMY OF MEDICINE, SECTION
OF PEDIATRICS

Chairman: Dr. Howard Craig, 175 E. 79th St., New York.
Secretary: Dr. Alfred E. Fischer, 73 E. 90th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHERN CALIFORNIA AFFILIATES

President: Dr. Crawford Bost, 400 Post St., San Francisco.
Secretary: Dr. William A. Reilly, 384 Post St., San Francisco.
Time: Second Thursday of September, November, January, March and May.

OKLAHOMA CITY PEDIATRIC SOCIETY

President: Dr. William M. Taylor, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 625 N. W. 10th St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Carl Fischer, Greene and Coulter Sts., Germantown, Philadelphia.
Secretary: Dr. Sherman Little, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday in January, March, May and November.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown, Pa.

Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh.

Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Stanley Meade, 913 Floyc Ave., Richmond, Va.

Secretary-Treasurer: Dr. Louise Galvin, 214 S. Boulevard, Richmond, Va.

Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Herbert Soule, 122 Rutgers St., Rochester, N. Y.

Secretary-Treasurer: Dr. Jerome Glaser, 390 S. Goodman St., Rochester, N. Y.

Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Jerome Diamond, 508 N. Grand Ave., St. Louis.

Secretary-Treasurer: Dr. Mary A. McLoon, 408 Humboldt Bldg., St. Louis.

Place: St. Louis Medical Society Bldg. Time: First Friday of each month from November to June.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Frederick B. Joy, Stimson Bldg., Seattle
Secretary: Dr. Sherod M. Billington, Medical Dental Bldg., Seattle.

Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Jeanette Harrison, 1136 W. 6th St. Los Angeles.

Secretary: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.

Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Campbell Harvey, 35 W. Huron St. Pontiac, Mich.

Secretary: Dr. Harry A. Towsley, University of Michigan, Department of Pediatrics and Communicable Diseases, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRICS SECTION (NEW YORK)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers N. Y.

Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.

Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.

INFECTIOUS LYMPHOCYTOSIS

DANIEL LEO FINUCANE, M.D., AND ROWLAND S. PHILIPS, M.D.

GLENN DALE, MD.

REVIEW OF THE LITERATURE

A condition in which there is marked total leukocytosis with high relative lymphocytosis and without clinical signs or symptoms has so far as we know been reported in the literature only 4 times previously. Three of these reports were of children, while 1 was of an adult.

In February 1941, Reyersbach and Lenert¹ reported under the title "Infectious Mononucleosis Without Clinical Signs or Symptoms" 16 cases occurring in a sanatorium for children who had had rheumatic fever. They were thought to be atypical cases of infectious mononucleosis, although they did not have any of its characteristics except lymphocytosis. The ages of the children varied from 6½ to 12 years. The leukocyte counts ranged from 18,400 to 59,300, with from 71 to 93 per cent of the cells lymphocytes. The Paul-Bunnell test, which is based on the fact that blood serum of patients with infectious mononucleosis clumps red cells of sheep in dilutions above the normal titer and which has been considered diagnostic of this disease, gave uniformly negative results. These authors also cited the case reported by Wilson and Cunningham² in 1929, of an adult aged 20 years, as the "only clearcut case" of marked leukocytosis without clinical signs or symptoms which had been reported previously.

Smith³ in August 1941 reported 2 more cases of high leukocytosis, with 44,900 and 98,000 as the maximum leukocyte counts and with lymphocytes 79 and 86 per cent respectively. The patients were children without clinical signs or symptoms, and the disease had the same characteristics as in the preceding cases. Smith pointed out that the disease described in the 2 previous reports was likely not infectious mono-

nucleosis at all, but was exactly similar to the disease in his 2 cases, which he termed "infectious lymphocytosis."

The fourth report, by Duncan,⁴ in September 1943, was of a child 4 years and 11 months old, with acute abdominal symptoms, headache, fever and a leukocyte count of 45,000 discovered at the onset. The maximum leukocyte count was 110,000, with 95 per cent of the cells lymphocytes. The differential cell count was similar to all of the preceding ones reported, the duration about five weeks and the reaction to the Paul-Bunnell test negative. This case differed from all of the others in the occurrence of acute symptoms at the onset.

REPORT OF CASES

It has been thought worth while to make the following report of an epidemic of 21 cases occurring in the children's wards of Glenn Dale Sanatorium, the tuberculosis sanatorium of the District of Columbia, during the winter of 1942-1943.

It is well known that pronounced total lymphocytosis is found in children with pertussis or with lymphatic leukemia, moderate lymphocytosis in children with infectious mononucleosis and only slight total or relative lymphocytosis in children with tuberculosis and with postinfectious conditions.

CASES 1 and 2.—The first of our patients, R. C., was a white boy aged 3 years, who had only a slight primary infection tuberculosis and was doing well. The leukocytosis was discovered on Nov. 25, 1942, while routine complete blood counts were being done on the children after a six month interval. Several other boys in the same room as this child had normal counts on the same day. Four of the blood counts for this patient follow, showing the pictures six months previously, five days after the first high count and (the maximum count) seventeen days after the first high count:

May 19, 1942: Erythrocytes 4,200,000, hemoglobin 63 per cent, or 10.5 Gm. per hundred cubic centimeters of blood, leukocytes 10,000, with lymphocytes 80 per cent, mononuclears 4 per cent, neutrophils, 16 per cent, eosinophils 0 and basophils 0.

4. Duncan, P. A.: Acute Infectious Lymphocytosis, *Am. J. Dis. Child.* **66**:267 (Sept.) 1943.

From the Medical Service of Glenn Dale Sanatorium.

1. Reyersbach, G., and Lenert, T. F.: Infectious Mononucleosis Without Clinical Signs or Symptoms, *Am. J. Dis. Child.* **61**:237 (Feb.) 1941.

2. Wilson, C. P., and Cunningham, R. S.: Consideration of Supravital Method of Studying Blood in Cases of Mononuclear Cell Response, *Folia haemat.* **38**:14 (March) 1929.

3. Smith, C. H.: Infectious Lymphocytosis, *Am. J. Dis. Child.* **62**:231 (Aug.) 1941.

Nov. 25, 1942: Erythrocytes 4,500,000, hemoglobin 75 per cent, or 12.5 Gm. per hundred cubic centimeters of blood, leukocytes 40,400, with lymphocytes 80 per cent, mononuclears 4 per cent, neutrophils 9 per cent, eosinophils 6 per cent and basophils 0.

blood, leukocytes 87,400, with lymphocytes 93 per cent, mononuclears 0, neutrophils 3 per cent, eosinophils per cent and basophils 0.

The stained smear showed small lymphocytes predominating, fewer large lymphocytes and a very few

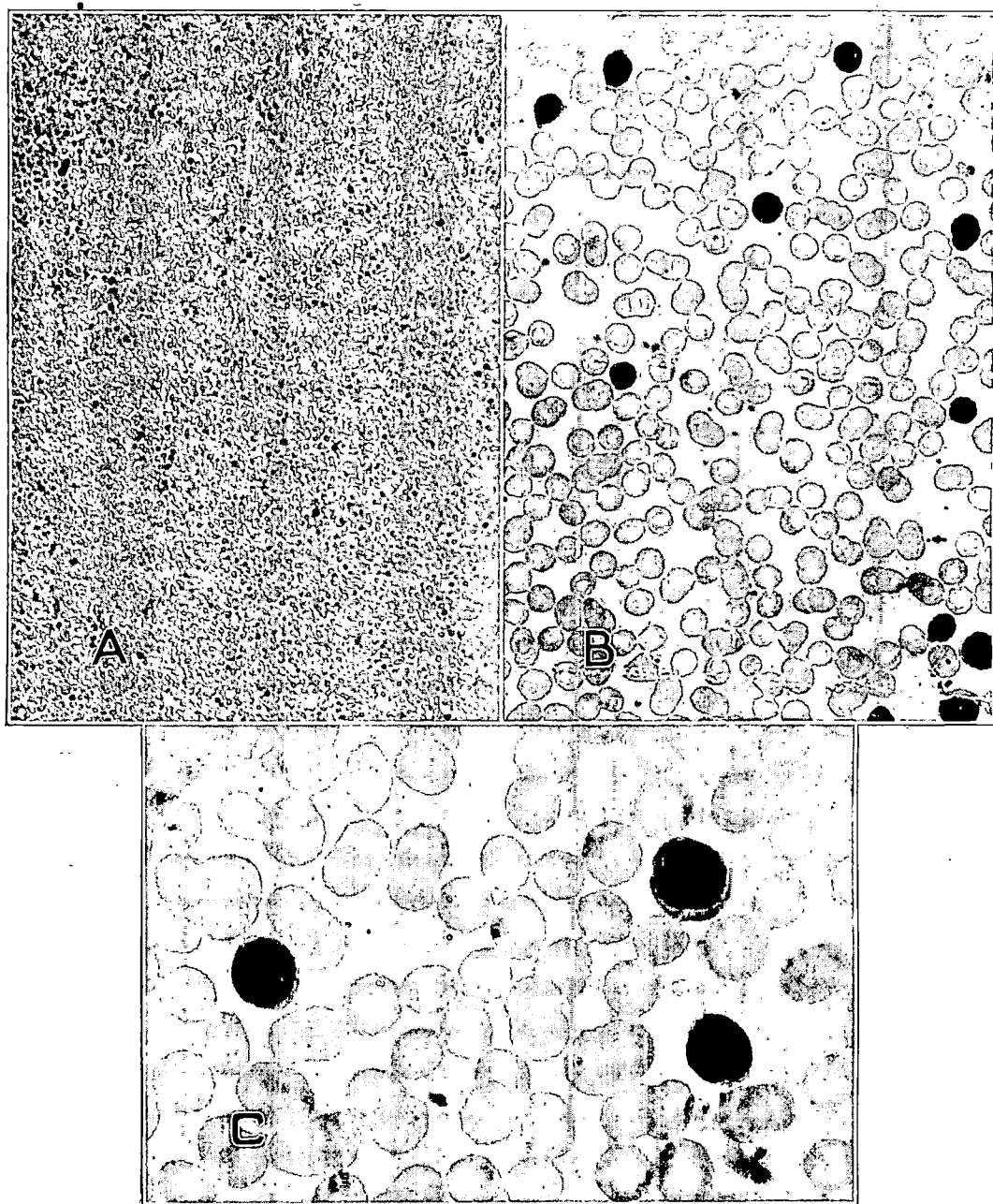


Fig. 1.—Blood picture in case 1: *A*, low power; *B*, high power; *C*, oil immersion, showing the great increase in normal-appearing lymphocytes.

Nov. 30, 1942: Erythrocytes 4,750,000, hemoglobin 57 per cent, or 9.5 Gm. per hundred cubic centimeters of blood, leukocytes 73,100, with lymphocytes 91 per cent, mononuclears 0, neutrophils 6 per cent, eosinophils 3 per cent and basophils 0.

Dec. 8, 1942: Erythrocytes 4,750,000, hemoglobin 54 per cent, or 9.0 Gm. per hundred cubic centimeters of

polymorphonuclears, eosinophils and monocytes. These were all well stained and normal looking, but in addition there were a few poorly stained degenerated or "smudge" cells, interpreted as degenerated lymphocytes. The erythrocytes seemed normal in appearance. The platelet count by the smear method on Dec. 1 was 171,000, which was not considered unusual (fig. 1, *A*

B and C). A pediatric consultation brought various opinions, and it was decided to observe the patient further.

On Dec. 8, 1942, the same day that the first patient, R. C., had his maximum count, another case of lympho-

On Dec. 10, 1942, the first patient, R. C., showed a slight drop of the leukocyte count, from 87,400 to 84,000, but the percentage of lymphocytes remained at 93 per cent. The second patient on this day had a rise in the number of leukocytes from 54,300 to 63,900,

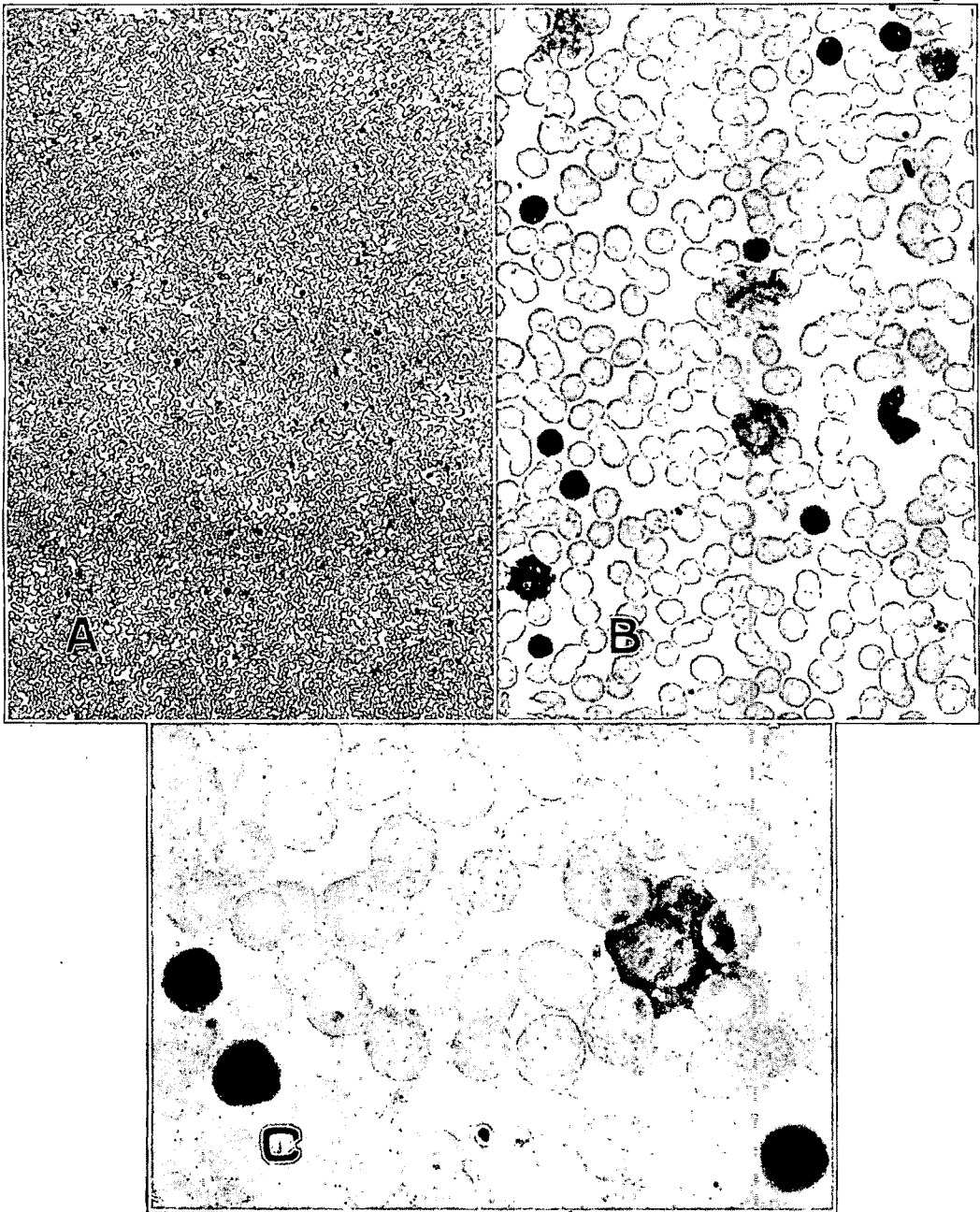


Fig. 2.—Blood picture in case 2, in which the highest total count of this series occurred: A, low power; B, high power; C, oil immersion, showing a picture similar to figure 1.

cytosis was discovered. The patient, W. McK., who was $4\frac{1}{2}$ years of age, had a leukocyte count of 21,300, with 83 per cent lymphocytes, in the morning and of 54,300, with 88 per cent lymphocytes, about six hours later. The stained smear had practically the same appearance as that in the previous case except that there were more "smudge" cells (fig. 2).

and the percentage of lymphocytes increased from 88 to 90 per cent. The platelets numbered 134,000.

The Paul-Bunnell, or heterophil antibody test was done on both patients the following day, Dec. 11, 1942. It gave negative results in both instances, i. e., positive agglutination only up to 1:32 for the first patient and up to 1:8 for the second.

From then on the leukocyte count and the percentage of lymphocytes of both of these patients gradually dropped to normal, the first more slowly than the second, with, however, a rise in the percentage of eosinophils, as follows:

R. C. on Jan. 12, 1943, forty-eight days after the onset: leukocytes 9,100, with lymphocytes 42 per cent, mononuclears 4 per cent, neutrophils 42 per cent, eosinophils 12 per cent and basophils 0.

W. McK. on Dec. 26, 1942, eighteen days after the onset: leukocytes 10,200, with lymphocytes 50 per cent, mononuclears 0, neutrophils 45 per cent, eosinophils 5 per cent and basophils 0.

three and after five months, in May and in July. In the first series of counts, started Dec. 18, 1942 and completed Dec. 28 there were discovered 15 additional cases. Three more cases were discovered later in this way, 1 on Jan. 4, 1943 and 2 on January 12. The last, or twenty-first, case was, strangely, detected by routine blood count on admission of the patient to the sanatorium from Washington, D. C. This patient's condition was at first suspected of being whooping cough, but plate tests were negative for the Bordet-Gengou bacillus, the cough improved and no cases of whooping cough developed in the institution. Furthermore, a roentgenogram of the chest revealed severe primary infection

Laboratory Data Concerning an Epidemic of Infectious Lymphocytosis

Case No.	Age, Yr.	Sex	Race	Approximate Date of Onset	Maximum Number of Leukocytes per Cu. Mm.	Percentage of Lymphocytes	Paul-Bunnell Test		Duration, Wk.
							Date	Result	
1	3	♂	W	11/25/42	87,400	93	12/11/42	Negative	7
							2/ 4/43	Negative	
2	4½	♂	N	12/ 8/42	63,900	90	12/11/42	Negative	2½
							2/ 4/43	Negative	
3	2	♂	N	12/18/42	43,900	73	12/24/42	Negative	3
							2/ 4/43	Negative	
4	2	♂	N	12/24/42	103,600	86	12/30/42	Negative	3
							2/17/43	Negative	
5	4½	♂	W	12/26/42	44,000	70	12/30/42	Negative	3
							2/ 4/43	Negative	
6	4½	♀	W	12/26/42	49,800	92	12/30/42	Negative	6
							2/25/43	Negative	
7	1½	♀	N	12/26/42	24,000	65	12/30/42	Negative	6
							3/ 9/43	Negative	
8	2½	♀	N	12/26/42	105,100	91	12/30/42	Negative	4
							3/ 9/43	Negative	
9	2	♀	N	12/26/42	120,000	97	12/30/42	Negative	6½
							3/ 9/43	Negative	
10	1½	♂	N	12/28/42	75,000	92	12/30/42	Negative	3
							2/17/43	Negative	
11	2	♂	N	12/28/42	41,800	83	12/30/42	Negative	8
							2/17/43	Negative	
12	2	♀	W	12/28/42	72,400	92	12/30/42	Negative	6
							2/25/43	Negative	
13	2½	♀	W	12/28/42	22,500	85	12/30/42	Negative	6
							2/25/43	Negative	
14	5½	♀	N	12/28/42	55,500	85	12/30/42	Negative	6
							2/25/43	Negative	
15	2	♀	N	12/28/42	42,900	62	12/30/42	Negative	6
							3/ 9/43	Negative	
16	2½	♀	N	12/28/42	62,000	75	12/30/42	Negative	3½
							3/ 9/43	Negative	
17	1½	♀	N	12/28/42	55,800	91	12/30/42	Negative	3½
							3/ 9/43	Negative	
18	2	♀	N	12/28/42	42,000	71	12/30/42	Negative	6
							3/ 9/43	Negative	
19	3	♂	W	1/12/43	68,600	91	1/13/43	Negative	4
							2/17/43	Negative	
20	2½	♂	N	1/12/43	79,800	73	1/13/43	Negative	4
							2/17/43	Negative	
21	1½	♂	N	2/25/43	32,300	93	2/25/43	Negative	3

The Paul-Bunnell test was repeated on Feb. 4, 1943, nearly a month after the last count had returned to normal, and again gave negative results in both instances.

Two subsequent counts at two month intervals were approximately the same, the last one, on May 17, 1943, revealing only slight further reductions. Soon afterward the first patient, R. C., was discharged from the sanatorium, in good health as far as could be determined.

OTHER CASES.—Because of the possibility that these 2 cases might be part of an epidemic occurring unnoticed, leukocyte and differential counts were then done again on all the approximately 100 children in the sanatorium. The counts were repeated at intervals of from five to fourteen days for about six weeks (through Feb. 10, 1943) and were done again after

tuberculosis with large peribronchial and hilar lymph nodes, which might easily have caused the cough by pressure reflex on the bronchi.

As can be seen from the table, the total leukocyte counts in all the cases ranged from 22,500 to 120,000 and the percentage of lymphocytes from 62 to 97 per cent. The last-named percentage occurred in the case in which there was the highest maximum total count. Figure 3 shows the course of the total leukocyte counts in the cases with the highest, the lowest and a median count. The blood pictures were similar in all cases and resembled those in the first 2 cases (figs 1 and 2). Persistent eosinophilia was noted in the majority of the cases, either at the height of the lymphocytosis or soon after the drop toward normal.

The Paul-Bunnell test was done in all of the cases of lymphocytosis, once during or slightly after the

height of the count and again a month or so after the highest count. It gave uniformly negative results in all cases; i. e., it gave positive agglutination only in dilutions of 1:16, 1:8 or 1:4, except in the first case in which a dilution of 1:32 also gave a positive result. It is evident that none of these results could be called positive. The repeat test was done to rule out infectious mononucleosis as the cause of this condition, since it has been stated that this test may give negative results during the acute stage and then become positive a month or so later.

Throat cultures were made of material from the throats of all the patients; they gave no clue to the cause of the condition. *Micrococcus catarrhalis* was present in all the patients. Other organisms found in order of frequency were: Friedländer's bacillus, *Pneumococcus*, *Bacillus influenzae* and *viridans* and other streptococci. All of the patients with lymphocytosis were isolated when discovered, those of the same sex and color being placed in one room.

Incidence.—The patients were almost evenly divided as to sex, as follows: girls, 11, 3 white and 8 Negro;

Examination of feces for intestinal parasites gave negative results.

In none of the patients were there observed enlarged cervical glands or palpable spleen, except in a few of the children in whom these conditions had been observed before as part of their primary tuberculous infection, and in no patient was there any additional enlargement. Furthermore, there was no sore throat or initial fever following a prodromal period of malaise, which is characteristic of infectious mononucleosis. These observations were confirmed by several consultants, including Dr. P. A. McLenden, of the Children's Hospital staff, Washington, D. C., and Drs. Michael L. Furcolow and Robert Olesen, of the United States Public Health Service, Bethesda, Md.

Stained blood specimens were examined by Dr. Hal Downey, of the University of Minnesota, and by Dr. Lester Newman, pathologist of Glenn Dale Sanatorium. Dr. Newman performed all of the Paul-Bunnell agglutination tests and examined all of the stained smears. Dr. Downey expressed the opinion that the blood smears did not resemble those obtained in infectious

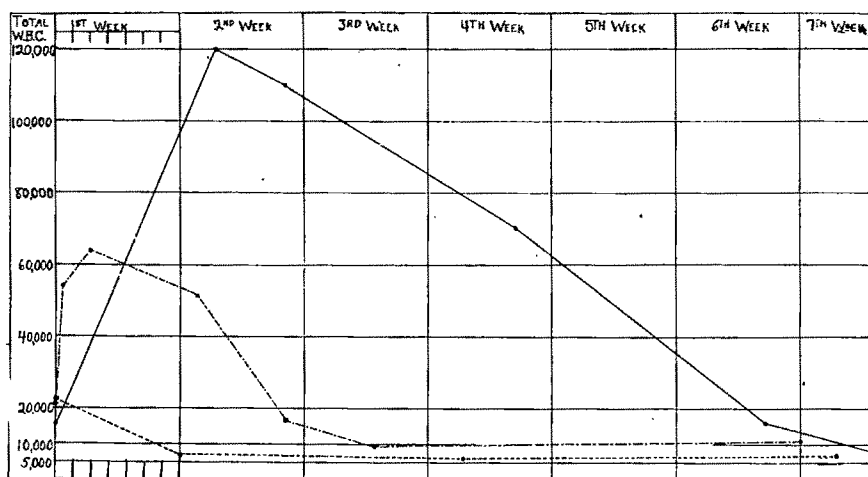


Fig. 3.—Course of 3 total leukocyte counts: highest count (—); lowest count (---), and a median count (---)

boys, 10, 3 white and 7 Negro. As the total ratio of Negro to white children of both sexes in the sanatorium was approximately 4:1, the figures just given would seem to indicate possibly a slightly greater susceptibility of the white children.

The majority of children were about 3 years old, the ages ranging from $1\frac{1}{2}$ to $4\frac{1}{2}$ except that there was 1 Negro girl aged $5\frac{1}{2}$ years.

Some of these children had severe primary tuberculous infections, as might be expected, but almost an equal number had only slight infections as was shown by roentgenograms of the chest.

In practically all the children in isolation nasopharyngitis developed toward the end of the period, after the total counts had started to drop toward normal. In several children this condition became severe. There were high fever and bronchitis and bronchopneumonia was threatened; the use of sulfathiazole or of sulfadiazine was required. During this period (from December to February) severe infections of the respiratory tract were common among the very young in the children's wards. Therefore, it is felt that these symptoms were coincidental rather than significant. A few of the very young girls had diarrhea for several days.

mononucleosis; they were more characteristic of chronic lymphatic leukemia. In cases of nonleukemic conditions, similar blood pictures are seen in whooping cough with as high a total count, but the percentage of lymphocytes is probably lower than in these cases. The practically negative results of heterophil antibody tests seemed to rule out, in his opinion, whatever is responsible for infectious mononucleosis.

Specimens of blood from some of the patients were examined by Dr. Michael Furcolow, of the United States Public Health Service, in an attempt to isolate a virus as the causative factor. His report follows: "No virus was isolated from any of these samples. Several samples were tested for virus-neutralizing antibodies against virus of lymphocytic choriomeningitis. No neutralizing antibodies were demonstrated."

DIFFERENTIAL DIAGNOSIS

In treating the condition described here as "infectious lymphocytosis", it seems important to us that a diagnosis be made as soon as possible. The three most important diseases to be dif-

ferentiated are infectious mononucleosis, lymphatic leukemia and pertussis.

Infectious mononucleosis has a clinical prodromal stage of malaise followed by an acute onset with fever, sore throat, pain in the back of the neck, enlargement and tenderness of the cervical lymph glands, enlargement of the spleen and the typical blood picture; the Paul-Bunnell test usually gives positive results sooner or later. Agglutination of sheep cells in dilutions of 1:56 to 1:112 is considered questionably a positive reaction, while agglutination of 1:160 or over is clearly positive. The blood picture is distinguished by lymphocytosis, which is usually not nearly so marked as in the condition described here. The stained smear shows the characteristic morphologic changes, i. e., the predominating abnormally large lymphocytic cells—often coarsely, less often finely, vacuolated—the deeply staining dense basophilic cytoplasm, with a more lightly staining perinuclear zone, and the fenestrated nuclei of heavy clumped chromatin or fine strands, staining lightly.

In infectious lymphocytosis, on the other hand, there is usually no discoverable clinical onset with fever and other symptoms, although this criterion can no longer be maintained absolutely since Duncan's report of his case in September 1943. The most important features are as follows: marked leukocytosis and high relative lymphocytosis, the counts reaching as high as 120,000 and 97 per cent respectively in our cases; the characteristic picture of the predominating small lymphocytes, normal in appearance except for the relatively few "smudge," or degenerated, cells in the stained smear, and the uniformly negative reaction to the Paul-Bunnell test in dilutions over 1:32.

Lymphatic leukemia in children is acute and rapidly progressive. It is always accompanied by anemia of varying degree and usually by a decrease in the number of platelets. In all cases there will be seen in the stained smears, with careful searching, evidence of the immaturity of the lymphocytes. They are large, round and uniform in size, with basophilic cytoplasm and large, lightly staining, finely granular nuclei, which contain nucleoli. In the aleukemic form there is leukopenia at the onset or throughout the disease; this form would seem to offer little difficulty in differential diagnosis. However, as was brought out by Falkenstein and Fowler,⁵ the leukemic form is the more frequent by far in children under 6 years of age, while the aleuke-

mic form is the more frequent in children aged 6 to 10 years, and the two forms are equally frequent between the ages of 10 and 15. In the leukemic form of the disease the leukocyte count may reach 300,000 to 400,000 or over, there are clinical signs and symptoms of enlarged lymph glands and spleen, fever, hemorrhages, cough, dyspnea and roentgen signs due to enlarged mediastinal lymph nodes. The average duration until death was only about eighteen weeks for the 61 cases reported by these authors.

Infectious lymphocytosis does not have these characteristics.

Pertussis may have a similar blood picture i. e., a leukocyte count of 100,000 or more cells with 90 per cent lymphocytes, but there are the characteristic clinical symptoms, and in a doubtful case the plate test will show the Bordet-Gengou bacillus growing on suitable mediums.

Slight or only relative lymphocytosis due to tuberculosis or postinfectious conditions can be accounted for by these conditions.

COMMENT

The question was raised by one of us whether the extreme lymphocytosis exhibited in these cases might not be beneficial in combating the tuberculosis. In none of the patients was the tuberculosis appreciably made worse by the lymphocytosis; several showed within three months an increased rate of improvement as indicated by roentgenograms of the chest, and some did not. Two patients who had previously had enlarged spleens showed a decrease in the size of the palpable spleen and an increased rate of clinical improvement within a three month period.

SUMMARY

Twenty-one cases of leukocytosis in children from 1½ to 5½ years of age are herewith reported; the leukocyte counts ranged from 22,500 to 120,000, with a relative lymphocytosis of 62 to 97 per cent. In the majority of cases the total counts were over 40,000, while in 3 they were over 100,000; in all except 4 instances the percentage of lymphocytes was 85 or over, and in these 4 it was 62 plus.

All of these cases except 1 occurred in epidemic form in the children's wards of Glen Dale Sanatorium, Glenn Dale, Md.; the other case was detected on admission of the patient to the sanatorium from Washington, D. C.

In none of the cases was there any symptom at the onset, the condition being discovered in every instance by routine blood counts.

5. Falkenstein, D., and Fowler, W. M.: Acute Lymphatic Leukemia in Childhood, *Am. J. Dis. Child.* 65:445 (March) 1943.

The average probable duration of the leukocytosis was approximately four and seven-tenths weeks, the longest seven weeks and the shortest two and one-half weeks.

In the majority of cases eosinophilia appeared as the total count began to drop. In a few this occurred during the highest count and persisted for seven months.

It is our impression that the cause of this condition is an infectious agent, but efforts to

demonstrate a bacterial or virus cause in these cases were fruitless.

Advice and assistance in the study of these cases was given by Dr. Hal Downey of the University of Minnesota, Dr. Michael L. Furcolow of the United States Public Health Service and the laboratory staff of Glenn Dale Sanatorium, under the direction of Dr. Lester Newman, pathologist, and including Miss Ruth Haines, Miss Ada Murphy and Mr. Bernard Lewis.

Glenn Dale Sanatorium.

HEREDITARY PERIODIC PARALYSIS IN A FAMILY SHOWING VARIED MANIFESTATIONS

C. P. OLIVER, PH.D.; MILDRED R. ZIEGLER, PH.D.,
AND IRVINE McQUARRIE, M.D.

MINNEAPOLIS

Periodic family paralysis is a relatively rare disease of human beings. In an extensive review of the literature on the subject, Talbott¹ stated that approximately 400 typical cases have been reported since Musgrave² first described a case in 1727.

The disease is characterized by the periodic development of acute flaccid paralysis, which usually begins in the extremities and progresses toward the trunk. The patient loses the power to move his limbs, but he can usually breathe, eat and speak freely, and the functions of his internal organs appear not to be disturbed. The deep reflexes of the affected extremities are absent at the height of the attack. After a period of time, usually a few hours, but in some instances two or three days, the patient recovers from the attack spontaneously. Another attack may occur within twelve to twenty-four hours or after a longer interval. During the attacks, the levels of serum potassium and inorganic phosphorus tend to be low, while during periods of freedom they are normal. The attacks usually occur during the latter part of the night or early in the morning and are often preceded by excessive exercise, fatigue or ingestion of an excess of carbohydrates during the previous day. Attacks can usually be induced in persons who have the potentiality for them by the administration of large amounts of carbohydrate or by the use of certain agents, such as insulin and epinephrine, which are known to lower the level of serum potassium.

The familial occurrence of periodic paralysis has been recognized, according to Talbott, since the report of Shakhnowitsch³ in 1882. Although both sporadic and familial instances of the disease have been reported in persons whose parents were normal, the instances due to heredity are usually considered to have resulted

from the transmission of a dominant trait. However, some of the atypical conditions reported to be periodic paralysis may have been due to extrinsic factors or to other disorders, complicated by a marked reduction in the serum potassium, which cause symptoms resembling those of periodic paralysis.

Even though the inheritability of periodic paralysis is well known, the family history to be reported here is of particular genetic importance because of the varying manifestations in the family. The affected members show many of the different expressions of the trait that are found when nonrelated affected persons are compared.

FAMILY HISTORY

The pedigree of family B, a family of Scandinavian ancestry 16 members of which have had periodic attacks of paralysis, is shown in the chart.

The propositus of family B (indicated on the chart by an arrow) is a normal-appearing boy, strong and healthy except for the intermittent attacks of flaccid paralysis. Typical attacks, which have been observed by the writer, begin acutely as "stiffness" of the muscles, but progress rather rapidly until he becomes helpless. He does not lose consciousness and is able to swallow and breathe without difficulty. On one occasion only have the respiratory muscles been involved. Within eight to twenty-four hours, the paralysis gradually disappears, leaving him with no apparent harmful after-effect. As many as three or four episodes of this character may occur during the week. At times, they have occurred daily. Attacks can be induced experimentally at will by feeding the patient 100 to 150 Gm. of dextrose, by injecting 30 to 50 units of insulin or by a combination of these procedures. They can be terminated by oral administration of 5 Gm. of potassium chloride dissolved in a glass of water.

The propositus has served as the subject of extensive metabolic studies at the University of Minnesota Hospital, the results of which will be reported separately. An elder brother (18 years of age) of the propositus has also been

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From the Departments of Pediatrics and Zoology and the Dight Institute for Study of Human Heredity, University of Minnesota.

1. Talbott, J. M.: *Medicine* 20:85, 1941.
2. Musgrave, W.: *Phil. Tr.*, London 3:33, 1727.
3. Shakhnowitsch: *Russk. Vrach* 32:557, 1882.

observed during his attacks. Genetic data on other members of the family have been collected by interviews or by correspondence with the parents and with each of the uncles and aunts of the *propositus*.

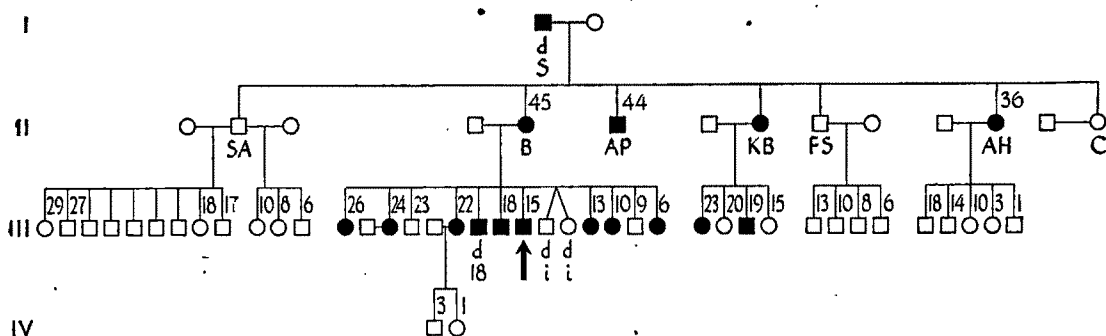
In this family, the trait behaves as a mendelian dominant character. The affected father in generation I transmitted the potentiality to one of his 3 sons and to 3 of his 4 daughters. One daughter, B, the mother of the *propositus*, has produced 13 children. Two of these died during infancy. Of the other 11, 9 have had one or more attacks of the paralysis. Another daughter, KB, has 2 children who have had attacks of the paralysis and 2 who have been free of attacks. The other affected daughter, AH, has 5 children, of whom none at the time of writing had yet had paralysis. However, 4 of the children are less than 16 years of age, and may yet have the disease. The affected son of generation II, AP, has no children.

None of the affected persons in family B came from nonaffected parents. In this family, there-

which are found when nonrelated families are compared. Data on various manifestations observed in the family are grouped in the table.

The most troublesome age periods are puberty and adolescence. In approximately 60 per cent of all cases reported the first attacks have come before the age of 16 years.¹ Some persons have the first paralytic attacks as early as the fourth year of life.⁴ In others, the first attack occurs as late as 40 years. The earliest onset in family B (table, column 4) was at the age of 4 years, and the latest, at 31, or possibly at 35 years if the statement of FS about S is correct. Six of the 16 affected members had the first attack during the first decade, 5 during the second decade, 2 after age 20 and 1 at either 19 or 35. Data regarding age at onset for 2 affected members are not available.

Attacks may occur every night over a period of time or only once or twice in a lifetime. Reports indicate that attacks usually become less frequent with age. However, Mitchell, Flexner and Edsall^{4b} reported that there was a long in-



Hereditary periodic paralysis: Family B.

Males are represented by squares and females by circles. Solid squares and circles represent persons who have had attacks of paralysis.

Roman numerals refer to generations. Arabic numerals refer to age in 1944. The letter *d* indicates death; an accompanying numeral gives the age at death; *i* refers to infancy.

fore, penetrance is complete, but the expression of the trait is varied. This variable manifestation suggests why in some of the hereditary cases the disease may seem to have skipped generations. Member AP, in generation II, had his first of three attacks at the age of 31; S, in generation I, had his first attacks, according to FS, at 35, although B stated that this person had his first attack at 19. The eldest daughter of B had her first attack at 24. The late ages of onset in some of the members and the variation observed in the other characteristics of the disease indicate that a potentiality may not always be expressed, because of extrinsic factors or of modifying (secondary) genes.

VARIED MANIFESTATIONS

The affected members of family B show many of the varied expressions of periodic paralysis

interval of freedom between the first and second attacks and that thereafter the attacks were more frequent. In 3 members of family B (column 6) the first attack was the only one in two years. Member AP had only three attacks in ten years. Some have had only two to five attacks a year, but others have them as often as two or three times each week. Member AH and the children of KB had frequent attacks at first, but their attacks became fewer with increasing age. AH reported that after her first paralysis she had one attack a month for about six years and then two or three a year for four years; she was then free of attacks for thirteen years, having had her latest attack in

4. (a) Biemond, A., and Daniels, A. P.: *Brain* **57**: 91, 1934. (b) Mitchell, J. K.; Flexner, S., and Edsall, D. L.: *ibid.* **25**:109, 1902.

1943. The children of KB had two or three attacks each week during the early period of the disease; they are now having fewer attacks.

As is shown by column 7 of the table, the affected members of family B differ considerably in the duration of the attacks. The paralysis in 1 person lasted only one or two hours. Four others had attacks of ten hours or less. Paralysis in 5 lasted from one to three days. In 2 others, the attacks lasted three to four days at the earlier ages, but according to their mother (KB), in more recent times the attacks have been of shorter duration. In the son of KB, at the time of writing the attacks occur late at night and are gone the next day, although he may become paralyzed again during the next night. This family, therefore, shows the same general behavior as that found when all cases of periodic

the use of his legs and finally became helpless. There is no way of knowing whether his condition was similar to that occurring in a family group described by Biemond and Daniels.^{4a} Muscular atrophy with periodic paralysis occurred in some of the members of that family. There is no evidence that the repeated periodic attacks have led to a more severe anomaly in members of this family, with the possible exception of S.

According to most reports, not only do the frequency and the severity of the attacks decrease with age, but the disease tends to disappear in late adult life. In the family history recorded by Biemond and Daniels, 4 of 14 affected members had supposedly reached the age of freedom from attacks. However, as is shown by family B, the freedom may be more

Varying Forms of the Periodic Attacks of Affected Members of the Family

Person *	Sex	Age in 1944	Age at First Attack	Age at Latest Attack	Number of Attacks During a Yr.	Duration of an Attack in Hr.	Comment
S.....	♂	Dead	19 or 31	"Did not lay him up"; became paralyzed
B.....	♀	45	9	32	52	48-72	
AP.....	♀	44	31	41	3 in 10 yr.	..	Slight attacks; only 3 attacks
KB.....	♀	No data
AH.....	♀	36	12	35	12 at first then 2 or 3 for 4 yr.	19 (last attack)	Interval of 13 years between last 2 attacks
B's children.....	♀	26	24	24	1	5	First attack only one in 2 years
	♀	24	6	24	52	24	
	♀	22	20	20	1	5	First attack only one in 2 years
	♂	Died 1942	..	18	Died during attack
	♀	18	8	18	200.	24-48	
	♀	15	7	15	100+	24-48	
	♀	13	11	12	2	4	
KB's children.....	♀	10	9	9	5	1-2	
	♀	6	4	4	1	48	First attack only one in 2 years
	♀	23	13	22	100+	72-96	Hard to breathe; painful
	♂	20	14	19	now 1-2 (now shorter)	100+ (now shorter)	
					now fewer (now varied)	72-96	Hard to breathe; painful

* The members are given in the order shown in the pedigree chart.

paralysis are compared. The average attack can be expected to last six to eight hours, although in some persons it may last as long as four days.

In some persons the attacks are severe, while in others they are very slight. It is also of interest that the disease seems to leave no ill after-effects in most persons. In family B most of the members do not complain of any difficulties as a consequence of the paralysis. The three attacks of AP have been slight. Member AH is able to "walk it off" when she has the prodroma, a condition also reported in a patient by Mitchell, Flexner and Edsall.^{4b} However, both affected children of KB are in pain during the attacks and find it difficult to breathe. One sibling of the propositus died in 1942 during a typical attack; death was due to paralysis of the respiratory muscles. According to one of his sons, S, in generation I, did not have severe attacks: They "did not lay him up." During the last twelve years of his life, however, S gradually lost

apparent than real. Most members of generation III are too young for the attacks to have discontinued, although the duration of the illness ranges from one to eighteen years. The mother of the propositus had the attacks for twenty-three years, but has had none during the past thirteen years. Member AH had also been free of the attacks for thirteen years when she had her latest attack in 1943. Subsidence of the condition, then, may not be permanent. The potentiality may be present, while the factors necessary to bring on the attacks may be less likely to occur in older persons. Whether the absence of the necessary factors is due to a change in the diet, a lack of strenuous exercise, or a change in the physiologic processes related to the muscles is not known.

COMMENT

Sixteen members of the family described in this study have had attacks of periodic paralysis.

The trait behaves as a simple mendelian dominant with complete penetrance but with varying manifestations.

In this one family, the affected members exhibit almost as many different expressions of the trait as are found among many nonrelated persons with this disease. The age of onset, as shown by the age at the first attack, ranges from 4 to 31, or possibly to 35 years, a variation as wide as that in the family described by Biernond and Daniels.^{4a} During a year, some members have only one or two attacks. Some of them, however, have one or more weekly. Although an attack tends to last for a few hours only in some of the members, some have attacks that last two to four days. In general, the attacks are not severe and have no harmful effects. However, 1 member died during an attack, and another, S, may have become paralyzed as a consequence of the attacks.

The extremely varied expression of the hereditary trait is observed when nonrelated persons who have attacks of periodic paralysis are compared. This suggests that extrinsic factors may be important in causing the wide differences among persons. However, the same diverse conditions are found among the 16 affected members of family B. In general, all of these members have lived the same kind of rural or small town life. Yet the manifestations have varied. It seems, therefore, that the variations may have been due in part, at least, to intrinsic factors. Sanders⁵ and also Biernond and Daniels^{4a} suggested that periodic paralysis and associated muscular atrophy in a family they described can be explained on the basis of two pairs of genes. A dominant gene of one pair is necessary for the occurrence of periodic paralysis, and one dominant gene of the other pair is necessary if muscular atrophy is to develop, but the gene for muscular atrophy is unable to function unless the gene for periodic paralysis is present. It is known that the paralysis is associated with a disturbed concentration of certain chemical constituents of the body fluids, especially potassium, and that the attacks tend to occur after a heavy meal of carbohydrates and after strenuous exercise. The change in frequency, intensity and duration of the attacks with increased age may be related to changes in habits of life. But it hardly seems likely that the differences among the younger members of family B can all be traced to differences in habits.

The data on family B give no evidence regarding the nature of the inherited anomaly which leads to the redistribution of potassium between

the blood and the tissues. Gardner⁶ and also Pudenz, McIntosh and McEachern⁷ referred to the condition as an inborn metabolic defect. Allott and McArdle⁸ considered the cause to be related to an abnormal neuromuscular apparatus.

The hereditary character of periodic paralysis might well be taken into account in studying the early and preclinical signs of the disease, particularly as regards a comparison of the chemical concentrations of the susceptible and nonsusceptible members of a family. In family B, however, only one sibship is available for study, and only 1 of the 2 nonaffected members of that sibship can be examined. An affected daughter of B has 2 young children, who by continued examination might provide some valuable information about the preclinical course of the disease.

SUMMARY

Sixteen members of a family are subject to attacks of periodic paralysis.

The trait behaves in this family as a mendelian dominant with full penetrance but with varied manifestations.

The manifestations, as shown by the age of onset, the frequency, duration and severity of the attacks and the duration of the disease, are as varied as those observed when nonrelated affected persons are compared.

The variability of the manifestations may be due in part to intrinsic factors.

DISCUSSION

DR. BENJAMIN KRAMER, Brooklyn: I wonder whether Dr. McQuarrie correlated the various effects of changes in diet and the intensity of the attacks with the potassium in the blood. As a rule, I think the attacks come on when the level of potassium is about 10 mg. or less per hundred cubic centimeters.

DR. IRVINE MCQUARRIE, Minneapolis: Yes. Serum potassium values were determined at fairly frequent intervals throughout the entire period of study. All attacks of paralysis were associated with reduced values, usually below 12 mg. per hundred cubic centimeters. During periods of freedom from attacks, normal levels were usually found. When the carbohydrate to potassium ratio of the diet approached the threshold for attacks, serum values fluctuated between 12 and 15 mg. per hundred cubic centimeters.

DR. BENJAMIN KRAMER, Brooklyn: Well, does it matter how the potassium fluctuates in the diet?

DR. IRVINE MCQUARRIE, Minneapolis: Our results indicate that wide fluctuations in the potassium content of the diet may be made without the occurrence of paralytic attacks so long as the carbohydrate to potassium ratio falls below certain levels. The last vary somewhat with the proportions of protein, carbohydrate and fat in the diet.

6. Gardner, H. W.: *Brain* **35**:243, 1912.

7. Pudenz, R. H.; McIntosh, J. F., and McEachern, D.: *J. A. M. A.* **111**:2253, 1938.

8. Allott, E. N., and McArdle, B.: *Clin. Sc.* **3**:229, 1938.

5. Sanders, J.: *Genetica* **16**:365, 1934.

SPORADIC INFECTIONS DUE TO SALMONELLA IN INFANTS

ERWIN NETER, M.D.

BUFFALO, N. Y.

The investigations of Kauffmann in Denmark, of Hormaeche and his collaborators in Uruguay and of Edwards, Schiff, Seligmann, Bornstein and Saphra in the United States have added substantially to the knowledge of the antigenic structure and the incidence of paratyphoid bacilli and of infections due to *Salmonella* in animals and in human beings. Certainly infections caused by *Salmonella* in human beings are more common than was believed even a few years ago, and vital statistics do not give a true picture of their prevalence. This is evident from a perusal of recent literature.

A number of reports have been published pertaining to epidemic outbreaks of salmonellosis in infants. Among others, McKinlay¹ described an epidemic of infectious diarrhea of the newly born. Unfortunately, the type of *Salmonella* responsible for the disease was not determined. Aballí, Falcón, Sala Panisello, Curbelo and Martínez Cruz² observed an outbreak of *Salmonella* aertrycke infection complicated by meningitis. Recently, Abramson, Frant and Oldenbusch³ reported several fatal cases of *Salmonella* Panama infection in babies 9 to 15 days of age. The infants in these cases were all cared for at the same nursery.

Except for reports of isolated cases, the literature on sporadic infections due to *Salmonella* in infants is limited. The most extensive investigation of the subject was carried out in Uruguay, by Hormaeche and his collaborators. A summary in English of their findings has been published recently.⁴ It is evident from their studies that

Salmonella organisms of various types are responsible for many instances of infantile summer diarrhea in that part of the world. Bornstein and Schwartz⁵ described 5 cases of sporadic infections due to *Salmonella* in infants. Four of the patients suffered from diarrheal disease; *S. typhi* murium was present in the feces of 2 infants and *Salmonella* Newport and *Salmonella* Montevideo in 1 infant each. The fifth patient had peritonitis due to *S. typhi* murium. Seligmann and Hertz⁶ reported 8 cases of infections due to *Salmonella* occurring in infants without fatality.

During the last three years 20 cases of *Salmonella* infections in infants have been observed at this hospital. In each instance the type of *Salmonella* organism involved was determined. A few unusual types were encountered. Since 4 of these cases ended fatally, it is evident that such infections are not always benign. The circumstances justify a report of the clinical and bacteriologic observations on these cases.

METHOD OF INVESTIGATION

Before the clinical aspects of the cases are described, brief mention will be made of the bacteriologic methods used in the investigation. Cultures of stools of all patients with diarrheal disease were made. The samples of feces were seeded on suitable mediums as soon as they were received in the laboratory. Endo, McConkey, *Salmonella*-*Shigella* and desoxycholate-citrate agar were used. During the last six months the enriching fluid of Bangxang and Eliot⁷ was also employed. Bismuth sulfite agar was included when indicated.

Lactose-nonfermenting colonies were fished from the agar plates after incubation at 37 C. for twenty-four and occasionally for forty-eight hours. Isolated strains were then tested for motility and for their action on dextrose, maltose, mannitol, lactose, sucrose, dulcitol, rhamnose, xylose, salicin and sorbitol. These test substances were employed in the form of a 1 per cent solution in phenol red (phenolsulfonphthalein) broth. Inverted tubes were used for the determination of the

From the Children's Hospital and the Department of Bacteriology and Immunology, University of Buffalo School of Medicine.

1. McKinlay, B.: Infectious Diarrhea in New Born Caused by Unclassified Species of *Salmonella*, *Am. J. Dis. Child.* **54**:1252 (Dec.) 1937.

2. Aballí, A. A.; Falcón, S.; Sala Panisello, F.; Curbelo, A., and Martínez Cruz, J. A.: *Salmonelosis del recién nacido*, *Bol. Soc. cubana de pediat.* **9**:123 (April) 1937.

3. Abramson, H.; Frant, S., and Oldenbusch, C.: *Salmonella* Infection of the Newborn: Its Differentiation from Epidemic Diarrhea and Other Primary Enteric Disorders of the Newborn, *M. Clin. North America* **23**:591 (May) 1939.

4. Hormaeche, E.; Surraco, N.; Pelttfo, C., and Aleppo, P.: Causes of Infantile Summer Diarrhea, *Am. J. Dis. Child.* **66**:539 (Nov.) 1943.

5. Bornstein, S., and Schwartz, H.: *Salmonella* Infection in Infants and Children, *Am. J. M. Sc.* **204**:546 (Oct.) 1942.

6. Seligmann, E., and Hertz, J. J.: *Salmonella* Infections, *Ann. Int. Med.* **20**:743 (May) 1944.

7. Bangxang, E., and Eliot, C. P.: An Investigation of Preserving Solutions for the Recovery of Dysentery Bacilli from Fecal Specimens, *Am. J. Hyg.* **31**:16 (Jan.) 1940.

formation of the gas. The strains were tested also for their ability to form indole. Agglutination tests were carried out with a few Salmonella serums available at this laboratory. Through the cooperation of Dr. Erich Seligmann, of the New York Salmonella Center, all strains were studied serologically and their type designation was established.

OBSERVATIONS

The table presents the pertinent data on the 20 cases of infection due to Salmonella in infants with respect to age, sex and race of the patients,

1 of these cases and also in 1 other case. Of the remaining 2 cases, 1 involved a carrier of Salmonella typhi murium with an infection of the upper respiratory tract and the other an infant who presented a feeding problem without diarrheal disease. The diagnosis of Salmonella infection in each of these cases was either based on or corroborated by the bacteriologic findings.

Salmonella organisms were isolated from feces in 19 cases. In the remaining case *S. typhi murium* was recovered from blood but not from

Sporadic Infections Due to Salmonella in Infants

Case	Age	Sex	Race	Diagnosis	Stool Culture	Blood Culture	Sulfonamide Compounds Given	Outcome
1	5 mo.	♂	W	Acute enterocolitis, bacteremia, phlebitis	—	<i>S. typhi murium</i>	Sth.	Died
2	6 mo.	♂	W	Acute enterocolitis	<i>S. typhi murium</i>	..	Sc.	Improved
3	1 mo.	♂	N	Acute enterocolitis, infection of upper respiratory tract, otitis media	<i>S. typhi murium</i>	..	Sc.	Improved
4	5 mo.	♂	W	Bacteremia, broncho-pneumonia	<i>S. typhi murium</i>	<i>S. typhi murium</i>	Sd.	Died
5	5 mo.	♂	W	Diarrhea, broncho-pneumonia	<i>S. typhi murium</i>	—	Sth. Sd. Sc.	Died
6	5 mo.	♂	W	Acute enterocolitis, laryngitis, eczema	<i>S. typhi murium</i>	..	Sth. Sc.	Improved
7	7 mo.	♂	W	Infection of upper respiratory tract, Salmonella carrier	<i>S. typhi murium</i>	..	S.	Improved
8	9 wk.	♂	W	Acute enterocolitis	<i>S. typhi murium</i>	..	Sc.	Improved
9	10 mo.	♂	W	Secondary anemia, diarrhea, otitis media, cervical lymphadenitis	<i>S. typhi murium</i>	—	Sth. Sc.	Improved
10	3 mo.	♂	N	Acute enterocolitis, otitis media, broncho-pneumonia	<i>S. typhi murium</i>	—	Sth.	Improved
11	3 mo.	♀	W	Acute enterocolitis	<i>S. typhi murium</i>	..	Sth. Sc.	Improved
12	11 days	♀	W	Acute enterocolitis, bronchopneumonia, peritonitis	<i>S. typhi murium</i>	—	..	Died
13	2½ mo.	♂	W	Acute enterocolitis, tetany	<i>S. typhi murium</i>	Improved
14	3 wk.	♂	W	Feeding problem; carrier	<i>S. typhi murium</i>	Improved
15	6 mo.	♀	W	Diarrhea, broncho-pneumonia, otitis media	<i>S. paratyphi B</i>	..	Sp.	Improved
16	9 mo.	♂	W	Diarrhea, secondary anemia	<i>S. paratyphi B</i>	—	Sd.	Improved
17	5 mo.	♀	W	Diarrhea, infection of upper respiratory tract	<i>S. urbana</i>	Improved
18	16 days	♀	W	Diarrhea	<i>S. london</i>	Improved
19	8 wk.	♂	W	Acute enterocolitis, tetany	<i>S. anatis</i>	Improved
20	4 mo.	♂	W	Diarrhea	<i>S. derby</i>	..	Sc.	Improved

* W, indicates white; N, Negro; S., sulfanilamide, Sp., sulfapyridine, Sth., sulfathiazole, Sd., sulfadiazine, Sc., succinylsulfathiazole; —, negative; .., observation not made.

clinical diagnosis, results of cultures of the stools and of the blood, treatment with sulfonamide compounds and outcome.

Of the 20 patients, 3 were less than 4 weeks old; their ages at the time of the onset of the illness were respectively 11, 16 and 21 days. Of the remaining infants, 4 were between 1 and 3 months, 8 between 3 and 6 months and 5 between 6 and 12 months of age.

The clinical diagnosis of enterocolitis, gastroenteritis or diarrheal disease was made in 17 cases. Paratyphoid bacteremia was present in

stools. Cultures of the blood were made in 7 cases. Salmonella organisms were recovered from the blood in 2 of these; in both instances *S. typhi murium* was the invading organism. The blood in the 5 other cases was sterile. The distribution of the various types of Salmonella was as follows: *S. typhi murium*, 14 cases; Salmonella paratyphi B, 2 cases, and Salmonella Urbana, Salmonella London, Salmonella Derby and Salmonella anatis, 1 case each.

Sixteen of the 20 cases ended in recovery and 4 in death. In 2 of the fatal cases bacteremia

from *S. typhi* murium was present. In the other 2 also the infection was due to *S. typhi* murium, the organisms being present in the intestinal tract.

None of the drugs used, including sulfathiazole, sulfadiazine and succinylsulfathiazole, was dramatically effective. Of 14 patients treated with one or more of these drugs 3 died and 11 recovered. There was 1 death among 6 infants who did not receive sulfonamide drugs. The 2 infants with bacteremia due to *S. typhi* murium were treated with sulfonamide compounds without any beneficial effect. Stools continued to contain pathogenic organisms in a number of cases during and following therapy with sulfonamide compounds, as for instance in case 20; previously described. It should be kept in mind that the various members of the *Salmonella* group differ in their susceptibility to treatment with sulfonamide compounds (Bornstein⁸).

A brief report of the fatal cases follows:

CASE 1.—A white boy 5 months old was admitted to the Children's Hospital because of vomiting and diarrhea which had begun one day previously. The condition developed two days after the child had been discharged from the hospital after treatment for eczema. During the present hospitalization his temperature ranged between 36 and 42 C. (96.8 and 107.6 F.). The diarrhea persisted, with up to twelve stools in twenty-four hours. Phlebitis was present. Sulfathiazole was administered to combat the infection, and because of dehydration, blood and fluids were given intravenously. Laboratory examinations resulted in the following pertinent findings: albuminuria; secondary anemia with a hemoglobin concentration which fell from 11 to 8 Gm. per hundred cubic centimeters of blood; a leukocyte count which ranged from 10,000 to 15,000; carbon dioxide-combining power of the plasma which varied from 25 to 50 volumes per cent; innumerable colonies of *S. typhi* murium on two consecutive cultures of the blood and absence of pathogenic organisms from the stools as demonstrated by two cultures. After a stay in the hospital of two and one-half weeks the patient died. Postmortem examination revealed the following conditions: serous hemorrhagic enterocolitis; generalized anemia with marked icterus, and considerable fatty degeneration and icterus of the liver.

CASE 4.—The other case of bacteremia due to *S. typhi* murium differed in many respects from the preceding one. The patient, a white boy 5 months old, had a history of a cold for four days prior to his admission. A clinical diagnosis of possible septicemia and pneumonia was made at that time. The child was given oxygen and sulfadiazine but died a few hours later. A culture of his blood taken during lifetime revealed innumerable colonies of *S. typhi* murium. The pertinent conditions noted at autopsy were as follows: confluent bronchopneumonia of both lungs and hemorrhagic mucoid bronchitis of both major bronchi. The intestine showed no abnormality. The possibility of a respiratory origin of the bacteremia was not investigated by means of cultural examinations of the bronchi and the lungs.

8. Bornstein, S.: The State of the *Salmonella* Problem, *J. Immunol.* 46:439 (June) 1943.

CASE 5.—A white boy was admitted to the Children's Hospital at the age of 5 months. The chief complaint was a cough and difficult breathing. A diagnosis of pneumonia was made during the stay at the hospital. The temperature ranged from 36 to 44.5 C. (96.8 to 108.1 F.). Diarrhea developed, and up to twenty stools were passed in twenty-four hour periods. In spite of the administration of blood plasma, 5 per cent solution of dextrose in isotonic solution of sodium chloride, sulfathiazole, sulfadiazine and succinylsulfathiazole, the severity of the illness progressed, and the patient died four weeks after admission. The pertinent laboratory findings were as follows: A leukocyte count varying between 14,000 and 43,000, *S. typhi* murium demonstrated in five out of six fecal cultures, a positive reaction to the Widal test in a dilution of 1:250 against the homologous strain and bacteriologically sterile cultures of the blood. Permission for postmortem examination was not obtained.

CASE 12.—An 11 day old white girl had a history of severe jaundice. Diarrhea and fever developed on the eleventh day of life. Cultures of the stools revealed the presence of *S. typhi* murium. A culture of the blood was sterile. The child died three weeks after admission to the hospital. The pertinent pathologic conditions noted on postmortem examination were: acute colitis with distention and superficial erosion, recent peritonitis and recent bronchopneumonia. The source of the infection could not be determined.

Because infections due to *S. London*, *S. Urbana*, *S. Derby* and *Salmonella anatis* are not common in infants, a summary of representative cases is herewith presented.

CASE 17.—A 5 month old infant was admitted to the hospital because of diarrhea and infection of the upper respiratory tract. Frank blood was present in the watery, greenish feces. The patient's temperature was 38.9 C. (102 F.). A clinical diagnosis of dysentery was made. His temperature rose to 39.5 C. (103.1 F.), and the diarrhea persisted. From the third day after admission the temperature was normal; the diarrhea stopped, and the infant began to gain weight. The patient was discharged one week after admission. *S. Urbana* was isolated from feces of this patient.

CASE 18.—A 16 day old white girl was admitted to the hospital because of diarrhea. The stools were watery and greenish but did not contain blood or mucus. The child vomited repeatedly. On her admission a diagnosis of diarrhea and marked dehydration was made. The temperature of the child during hospitalization varied between 36.2 and 40 C. (97.16 and 104 F.). The infant was given 5 per cent dextrose in isotonic solution of sodium chloride intravenously. The diarrhea persisted, five to seven stools being passed in twenty-four hour periods. The temperature, however, returned to normal. Two specimens of feces obtained during hospitalization revealed the presence of *S. London*. The source of infection could not be determined. The patient was discharged for treatment by a private physician.

CASE 19.—An 8 week old white boy was admitted to the hospital because of convulsions. His temperature on admission was normal. There was no diarrhea. The level of blood calcium on his admission was 6 mg. per hundred cubic centimeters. One week later diarrhea developed, up to ten stools being passed daily, and the patient's temperature rose to 39.8 C. (103.6 F.). There was no blood in the feces. Conservative treatment resulted in recovery from the diarrheal disease. A cul-

ture of the stool revealed the presence of *S. anatis*. The mother of the child did not harbor this organism in her stool.

CASE 20.—A 7 month old white boy had diarrheal disease which resulted in marked dehydration. Up to nine stools were passed in twenty-four hour periods. Blood was not present in the feces. The temperature reached 39.2 C. (102.6 F.) The child was given succinylsulfathiazole. One week later the temperature returned to normal and the diarrhea subsided. *S. Derby* was present in the feces over a period of more than five weeks. It is interesting that for three weeks the child (weighing 21 pounds [9,525 Gm.]) received as much as 9 Gm. of succinylsulfathiazole per day and that this treatment failed to eliminate the *Salmonella* organisms from the intestinal tract and there was almost no reduction in the number of coliform organisms in the feces.

COMMENT

Infections due to salmonella in infants occur both epidemically and sporadically. Clinical manifestations are of several different forms: (1) paratyphoid, resembling typhoid and also referred to as salmonella fever; (2) septicemia and bacteremia, often associated with purulent lesions, such as arthritis, osteomyelitis, meningitis and others; (3) gastroenteritis, enterocolitis and food poisoning.

Incidence.—The 20 cases of sporadic infections due to *Salmonella* in infants under 1 year of age reported in this communication present several features worthy of discussion. Since the cases were observed over a period of approximately three years, it is evident that sporadic salmonellosis of infants is not a very rare disease in this part of the country. At this hospital infections due to *Salmonella* have greatly exceeded infections due to *Shigella* during the last few years. The true incidence of salmonellosis is not known. In part this is due to the fact that adequate bacteriologic examinations are not always carried out. It should be noted that infections due to many types of *Salmonella* are not reportable in some localities, for example, in the state of New York. That a definite need for more information on the incidence of *Salmonella* infections in man exists cannot be doubted.

Clinical Features.—The main clinical syndromes encountered in the 20 cases of sporadic infections due to *Salmonella* in infants were as follows: gastrointestinal disorders (gastroenteritis, enterocolitis, diarrheal disease), 17 cases; septicemia or bacteremia due to *Salmonella*, 2 cases. Severe hemorrhagic enterocolitis was found on postmortem examination in 1 of the bacteremic infants; in the other, intestinal lesions were absent.

In the 2 remaining cases it is doubtful whether the presence of *Salmonella* organisms in the intestinal tract had any relation to the clinical manifestations. In 1 of these cases the patient

had an infection of the upper respiratory tract of unknown cause; in the other there was a feeding problem. It is likely that these patients were carriers of *Salmonella* organisms, particularly since there was neither evidence nor history of diarrheal disease.

Hormacche and his associates⁴ offered the following classification of *Salmonella* infection of the intestinal tract: (1) salmonellosis associated with enteritis and (2) salmonellosis not associated with enteritis. The enteritis may be choleraform, dysenteriform or mixed. That the infection may produce a clinical picture of dysentery is borne out by case 17. This patient had fever and diarrhea; blood was present in the feces. *S. Urbana* was recovered from the stools.

Worthy of note is the observation that in 8 cases of salmonellosis of the alimentary tract inflammatory lesions outside of the intestine were also present, particularly infections of the upper respiratory tract, pneumonia and otitis media. Since a special search for *Salmonella* organisms in these lesions was not made, it is impossible to state whether or not these organisms were also responsible for the parenteral infection. It is conceivable that in some instances two concurrent diseases of different origin were present. It is also possible that the parenteral infection lowered the resistance of the patient and thus enabled the paratyphoid bacilli already present in the intestinal tract to produce the diarrheal disease. Further studies on the relationship of parenteral infections to diarrhea due to *Salmonella* in infants are needed.

Distribution.—So far as the distribution of the various types is concerned, *S. typhi* murium was encountered in 14 cases, *S. paratyphi* B in 2 and *S. London*, *S. Urbana*, *S. Derby* and *S. anatis* in 1 case each. For comparative purposes the data, collected by Bornstein, on the distribution of the various types of *Salmonella* in 500 cases of infection in human beings from North America and Cuba should be cited. *S. typhi* murium was encountered in slightly more than 30 per cent of the 500 cases. In the series reported here this type was found in 14 of 20 cases, or approximately 70 per cent. Bornstein encountered *S. anatis* in 2.6 per cent, *S. Derby* in 2.2 per cent and *S. Urbana* in 0.6 per cent of the cases and *S. London* not at all. Data on infections in infants caused by these rather unusual types have been included in the present paper. In all instances these organisms were responsible for diarrheal disease. *S. Urbana* caused a dysentery-like picture.

Therapy.—Four of 20 patients died; so it is evident that *Salmonella* infections in infants are not necessarily mild. Unfortunately, treatment

with sulfonamide compounds has not yielded encouraging results. Such drugs did not prevent a fatal outcome in 3 cases; so little can be said with respect to the efficacy of sulfonamide compounds in the treatment of sporadic infections of infants due to *Salmonella*. No hope can be placed in penicillin, since this drug seems to be ineffective against gram-negative enteric organisms. It is possible, however, that other antibiotic substances may be found which will be active against *Salmonella*.

The prevention of infections due to *Salmonella* becomes more important in view of the fact that effective specific therapy is not available at the present time. Unfortunately, little is known concerning the source of the infection in sporadic cases. Studies on this subject are needed.

SUMMARY

Clinical and bacteriologic data on 20 sporadic cases of infection due to *Salmonella* in infants (under 1 year of age) are presented. The pertinent observations were as follows:

Seventeen infants had infection of the intestinal tract due to *Salmonella* (gastroenteritis, enterocolitis and diarrheal disease). In 2 instances the paratyphoid bacillus was recovered from feces. One of the patients presented the clinical picture of dysentery. In 8 patients parenteral infections (pneumonia, otitis media and others) of undetermined cause were also present.

Two infants had bacteremia due to *Salmonella*. *S. typhi* murium was the invading organism.

Both patients succumbed. One of them had severe hemorrhagic enterocolitis; the other presented no evidence of intestinal disorder.

Two patients, respectively 3 weeks and 7 months old, were carriers of *Salmonella*: *S. typhi* murium was recovered from feces.

The distribution of the 20 patients as to age was as follows: less than 4 weeks old, 3 infants; between 1 and 3 months, 4; between 3 and 6 months, 8, and between 6 and 12 months, 5. Five infants were girls, and 15 were boys. Eighteen were white, and 2 were Negro.

The following types of *Salmonella* were encountered: *S. typhi* murium in 14 cases, *S. paratyphi* B in 2 cases and *S. Urbana*, *S. Derby*, *S. London* and *S. anatis* in 1 case each.

Of the 20 infants 16 recovered and 4 died. Two of the infants who died had bacteremia due to *S. typhi* murium; the other 2 had infection of the intestinal tract due to *S. typhi* murium.

Fourteen infants were treated with sulfonamide compounds, including sulfathiazole, sulfadiazine and succinylsulfathiazole. Of these 3 died and 11 recovered. There was 1 death among 6 infants who did not receive sulfonamide compounds. These drugs failed to eliminate the *Salmonella* organisms from the intestinal tract in several instances.

Brief reports are presented of the fatal cases and of those in which the infection was due to rather unusual types (*S. London*, *S. Derby*, *S. anatis* and *S. Urbana*).

219 Bryant Street.

HEMOLYTIC DISEASE OF THE FETUS AND THE NEWBORN INFANT

WITH SPECIAL REFERENCE TO TRANSFUSION THERAPY AND THE
USE OF THE BIOLOGIC TEST FOR DETECTING RH SENSITIVITY

A. S. WIENER, M.D.; I. B. WEXLER, M.D., AND E. GAMRIN, M.D.

BROOKLYN, N. Y.

The Rh factor of Landsteiner and Wiener¹ has been shown to be related to about 90 per cent of the reactions to intragroup blood transfusion² and to about 90 per cent of the cases of erythroblastosis (hemolytic disease of the fetus and of the newborn).³

In the typical case, the patient having a hemolytic reaction to an intragroup transfusion or the mother delivered of an erythroblastotic infant is found to have Rh-negative blood. However, since only 1 in about 25 to 50 persons with such blood is readily sensitized to the Rh factor, either by transfusion or by pregnancy, the mere fact that the patient's blood is Rh negative is not proof that the Rh factor is responsible for the pathologic state. One must prove in addition that sensitization to the Rh factor has occurred.

From the Blood Transfusion Division and the Departments of Pediatrics and Obstetrics of the Jewish Hospital.

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1. Landsteiner, K., and Wiener, A. S.: An Agglutinable Factor in Human Blood Recognizable by Immune Sera for Rhesus Blood, *Proc. Soc. Exper. Biol. & Med.* **43**:223 (Jan.) 1940. Landsteiner, K., and Wiener, A. S.: Studies on an Agglutinin (Rh) in Human Blood Reacting with Anti-Rhesus Sera and with Human Isoantibodies, *J. Exper. Med.* **74**:309 (Oct.) 1941.

2. Wiener, A. S., and Peters, H. R.: Hemolytic Reactions Following Transfusions of Blood of the Homologous Group, with Three Cases in Which the Same Agglutinin Was Responsible, *Ann. Int. Med.* **13**:2306 (June) 1940. Wiener, A. S.: Hemolytic Reactions Following Transfusions of Blood of the Homologous Group: Further Observations on the Role of Property Rh, Particularly in Cases Without Demonstrable Isoantibodies, *Arch. Path.* **32**:227 (Aug.) 1941.

3. Levine, P.; Katzin, E. M., and Burnham, L.: Isoimmunization in Pregnancy: Its Possible Bearing on the Etiology of Erythroblastosis Fetalis, *J. A. M. A.* **116**:825 (March 1) 1941. Burnham, L.: The Common Etiology of Erythroblastosis and Transfusion Accidents in Pregnancy, *Am. J. Obst. & Gynec.* **42**:389 (Sept.) 1944. Levine, P.; Burnham, L.; Katzin, E. M., and Vogel, P.: Role of Isoimmunization in the Pathogenesis of Erythroblastosis Fetalis, *Am. J. Obst. & Gynec.* **42**:925 (Dec.) 1941.

TESTS FOR SENSITIVITY TO THE RH FACTOR

Tests in General Use.—The usual method of demonstrating Rh sensitivity is to test the patient's serum for anti-Rh agglutinins, as was first done by Wiener and Peters.² However, it was soon discovered that there is a high percentage of persons with Rh-negative blood who are highly sensitive to the Rh factor (as proved by the occurrence of hemolytic reactions to intragroup transfusion or by the birth of an infant with hemolytic disease) whose plasma does not contain any demonstrable anti-Rh agglutinins. These puzzling cases have been explained, at least in part, by the discovery that in addition to Rh antibodies that produce hemagglutination there are Rh antibodies characterized by their ability to combine specifically with Rh-positive cells without producing a visible reaction.⁴ If Rh-positive blood is mixed with serum containing antibodies of the latter type, the blood loses its capacity to be agglutinated even by extremely potent anti-Rh agglutinating serums, presumably because all the combining sites on the erythrocytes have been occupied. Because of this property of blocking the action of anti-Rh agglutinins, the new type of antibody has been named the blocking antibody. The Rh-blocking antibodies appear to be of greater clinical significance than the agglutinating antibodies, and their discovery has served to explain the hitherto puzzling lack of correlation between the titer of anti-Rh agglutinins and the severity of the disease in the infant. Thus, severe or fatal icterus gravis has occurred although the maternal serum contained no demonstrable anti-Rh agglutinins, and at least 1 case⁵ has been reported in which a mother with Rh-negative blood whose serum contained anti-Rh agglutinins in high titer gave birth to a normal infant with Rh-positive blood.

4. Wiener, A. S.: A New Test (Blocking Test) for Rh Sensitization, *Proc. Soc. Exper. Biol. & Med.* **56**:173 (June) 1944.

5. Dockeray, G. C., and Sachs, H.: Rh Antibodies in the Maternal Circulation Without Clinical Manifestations of Erythroblastosis in the Child, *J. Immunol.* **48**:213 (April) 1944.

The Biologic Test for Sensitivity.—A third method of detecting Rh sensitivity, namely, a biologic test, was described by one of us (A.S.W.⁶) in 1942. This test has proved particularly useful for the prevention of hemolytic reactions to intragroup transfusion in the absence of the facilities or the time for carrying out tests for the Rh factor. The biologic test consists of intravenous injection of 50 cc. of blood to which the patient may be sensitive and comparison with the naked-eye of the color of the patient's original citrated plasma with that of a comparable specimen taken one to one and one-half hours after the injection. If sensitivity is present, the second sample of plasma will be distinctly darker and not infrequently the patient will have a chill fifty to sixty minutes after the test is started, followed by a rise in temperature. In case of doubt an additional 50 cc. of blood may be injected and a third specimen of the patient's plasma obtained for comparison after one more hour. If the reaction to this test is negative, any quantity of blood from the same donor can be given without untoward effect.

The purpose of the present paper is principally to describe some experiences with the application of the biologic test for the detection of sensitivity to the Rh factor caused by pregnancy and at the same time to present some recent observations on the transfusion therapy of hemolytic disease of the newborn.

REPORT OF CASE

CASE 1.—Obstetric History.—A couple gave the following obstetric history:

First pregnancy (1937), abortion at one month.

Second pregnancy (1938), normal female child.

Third pregnancy (1940), full term child, normal except for asthma, eczema and hives.

Fourth pregnancy (1941), abortion at two months.

Fifth pregnancy (1942), 3½ month fetus which underwent hydatidiform degeneration.

Sixth pregnancy (1942), miscarriage at four and one-half months.

This couple was extremely anxious to have more children, and the wife had taken courses of progesterone and thyroid. Throughout the sixth pregnancy she had remained in bed.

Results of Grouping Tests.—The referring physician suggested that the Rh factor might be related to the abortions, and tests of the blood yielded the following information:

Blood of	Group and Subgroup	Rh type ⁷
Husband	A ₁	Rh ₂
Wife	A ₁	Negative

6. Wiener, A. S.: *Blood Groups and Transfusion*, ed. 3, Springfield, Ill., Charles C Thomas, Publisher, 1943, p. 71.

7. The Rh-positive type includes a number of distinct varieties of blood, because of the existence of more than one kind of Rh factor. Five principal varieties have been identified; they are designated as Rh₁,

Results of Biologic Tests.—Because the wife's blood was Rh negative, the referring physician felt that sensitization to the Rh factor had probably occurred. However, in the experience of the authors and of most other workers, the Rh factor is not related to early abortions. Rh isoantibodies could not be demonstrated in the woman's serum, but, as has already been mentioned, this fact does not necessarily rule out sensitivity; so further studies were deemed necessary.

Accordingly, 50 cc. of the husband's blood was mixed with 100 cc. of isotonic solution of sodium chloride and slowly injected into a vein of the wife by the gravity method. There was no reaction of any sort to the procedure, and the wife's plasma one hour after the transfusion was no darker than the plasma withdrawn before the transfusion, indicating that no hemolysis had occurred. This result proved that the woman was not sensitive to the Rh factor and that the repeated early abortions had a cause other than isoimmunization.

CASE 2.—Obstetric History.—A man of 48 years and a woman of 35 years, who had been married for ten years, gave the following obstetric history:

First pregnancy (1937), full term stillbirth, attributed to a knot in the umbilical cord.

Second pregnancy (1939), induced abortion in the third or fourth month.

Third pregnancy (1941), full term infant who died after thirty-six hours. Death was attributed to premature separation of the placenta with resulting cerebral anoxemia and irremediable damage to the brain. The nurse had called the physician's attention to the extreme pallor of the infant one hour before death. No jaundice was noted at any time.

Fourth pregnancy (1942), premature stillbirth in the seventh month. An autopsy was performed, but threw no light on the cause of death.

Results of Grouping and Rh Tests.—Tests had been made for the Rh factor: The husband's blood was found to be Rh positive and the wife's Rh negative. We were requested to give the prognosis for future pregnancies, because the couple was anxious to have a child.

Complete serologic tests gave the following information:

Blood of	Group and Subgroup	MN Type	Rh Type
Husband	A ₁	MN	Rh ₁ Rh ₂
Wife	O	N	Negative

No anti-Rh agglutinins could be detected in the wife's serum, but the obstetric history was so suggestive that we felt that the woman was nevertheless sensitized to the Rh factor.

Rh₂, Rh₀, Rh' and Rh". According to the theory proposed by A. S. Wiener (*Genetic Theory of Rh Blood Types*, Proc. Soc. Exper. Biol. & Med. **54**:316 [Dec.] 1943), these Rh factors give rise to eight Rh blood types (phenotypes), which are inherited through a series of allelic genes, Rh₁, Rh₂, Rh₀, Rh', Rh" and rh, each gene being named for the property which it determines. For full details consult the following papers: Wiener, A. S.; Sonn, E. B., and Belkin, R. B.: *Heredity of the Rh Blood Types*, J. Exper. Med. **79**:235 (March) 1944. Wiener, A. S.: *Nomenclature of the Rh Blood Types*, Science **99**:532 (June 30) 1944. Race, R. R.; Taylor, G. L.; Cappell, D. F., and McFarlane, M. N.: *Recognition of a Further Common Rh Genotype in Man*, Nature, London **153**:52 (Jan. 8) 1944.

Results of Biologic Test.—To settle the question definitely a biologic test was done. Fifty cubic centimeters of group O, Rh₁ Rh₂ blood from a professional donor⁸ was injected into a vein of the woman by syringe. Within fifty minutes the patient experienced a slight chilliness, which became a definite chill in another fifteen minutes. Blood plasma procured at this time was noticeably darker than that obtained before the injection. (The icterus index had risen from 4 to 6 units.) The chills continued intermittently for another hour, and the patient complained of faintness. Since she had not eaten for five hours, she was given a glass of orange juice, which she vomited. She complained of abdominal cramps and fainted on attempting to go to the bathroom. She was readily revived, but her blood pressure at this time was only 70 mm. systolic. An intravenous infusion of 250 cc. of 10 per cent dextrose in isotonic solution of sodium chloride mixed with 50 cc. of 3 per cent sodium citrate was rapidly administered, and at the same time another sample of blood was withdrawn. The icterus index had by now risen to 8 units. After the intravenous infusion and a hypodermic injection of 5 minims (0.3 cc.) of 1:1,000 solution of epinephrine hydrochloride the patient felt markedly improved, and after drinking a cup of black coffee she felt well enough to leave the office.

The positive reaction to the biologic test proved that the patient was sensitive to the Rh factor, despite the absence of demonstrable Rh antibodies in her serum. It is significant that a sample of her serum obtained one week after the biologic test was found to contain blocking antibodies but no demonstrable anti-Rh agglutinins. Since the husband's blood belongs to type Rh₁ Rh₂, this couple can have only children with Rh-positive blood (presumably half of them with type Rh₁ and half with type Rh₂). Except in the unlikely event of spontaneous desensitization, there is no chance of a normal infant's resulting from this mating.

The severity of the symptoms which the patient in this case experienced after the injection of 50 cc. of Rh-positive blood convinced us that the following precautions are advisable when biologic tests are being performed: First the test should, if possible, be carried out in a hospital. Second, when the clinical history suggests that marked sensitivity may be present, the test dose should be given well diluted with isotonic solution of sodium chloride and should be administered by the drip rather than by the syringe method. If one desires to be extremely cautious, fractional doses given over a period of one to two hours may be used.

CASE 3.—Obstetric History.—The patient had had one preceding pregnancy, two years previously, which resulted in a full term male infant delivered by cesarian section. The section was necessary because of pelvic

8. The husband could not be used because his blood was of an incompatible group. Care was taken to use a professional donor with blood of the same Rh type as that of the husband.

disproportion and an incipient Bandl ring. This baby appeared normal at birth, but at 5 days anemia, hepatomegaly and splenomegaly were noted. Blood studies showed a red blood cell count of 1,900,000 cells with 58 per cent hemoglobin, and there were occasional normoblasts on the smear. The infant was given four transfusions, totaling 260 cc. of blood, over a period of two weeks, but when he was discharged his hemoglobin was still only 50 per cent and the red cell count 2,700,000. No account was taken of the Rh factor in selecting the donors for the transfusions. At home the infant was given hepatic therapy, and he gradually improved. At the time of writing he was entirely normal.

The mother was referred for study because she was pregnant again and near term, and it was felt there was a high probability that the new infant would also have hemolytic disease.

Results of Grouping Tests.—Blood tests of the family showed the following:

Blood of	Group	MN Type	Rh Type
Father	O	MN	Rh ₁
Mother	O	N	Negative
Son (2 years old)	O	MN	Rh ₁

Prognosis.—Although no anti-Rh agglutinins could be demonstrated in the maternal serum, these findings supported the diagnosis of erythroblastosis in the first child and made it probable that the expected infant would also have hemolytic disease.⁹ It was planned to deliver the infant by cesarian section, and arrangements were made to give the infant a complete exsanguination transfusion with Rh-negative blood as soon as it was born.

Procedures.—On the morning chosen for the operation, a biologic test was performed on the mother by injecting 50 cc. of her husband's blood intravenously. After fifty minutes, the patient had a severe chill lasting twenty minutes, and a sample of her blood plasma taken at that time was distinctly darker than the plasma obtained before the injection. This confirmed the impression that the patient was sensitive to the Rh factor. Rh-negative, group O blood¹⁰ was then drawn from a donor in preparation for the exsanguination transfusion.

As soon as the infant, a girl, was delivered through the incision, it was noticed that she was extremely pale, rather than icteric, and seemed listless. A blood count was ordered at once, but before the technician had time to arrive the baby's condition became noticeably worse. Her breathing became shallow and rapid; she did not respond to strong stimuli, and within a few moments she appeared moribund. Since all the apparatus and the blood were at hand, a transfusion was started at once with the aid of a syringe-valve set. Eighty cubic centimeters of blood was administered rapidly, and the infant's color and her condition improved dramatically. The hemoglobin was deter-

9. Unfortunately no anti-Hr (St) serum was available at the time these tests were made. As R. R. Race and G. L. Taylor (A Serum That Discloses the Genotype of Some Rh-Positive People, *Nature*, London **152**:300 [Sept. 11] 1943) pointed out for the first time, if blood of a type Rh₁ parent reacts negatively with a strong St serum he or she cannot have Rh-negative children.

10. In this case we knew that the infant's blood would belong to group O because that of both parents belonged to group O.

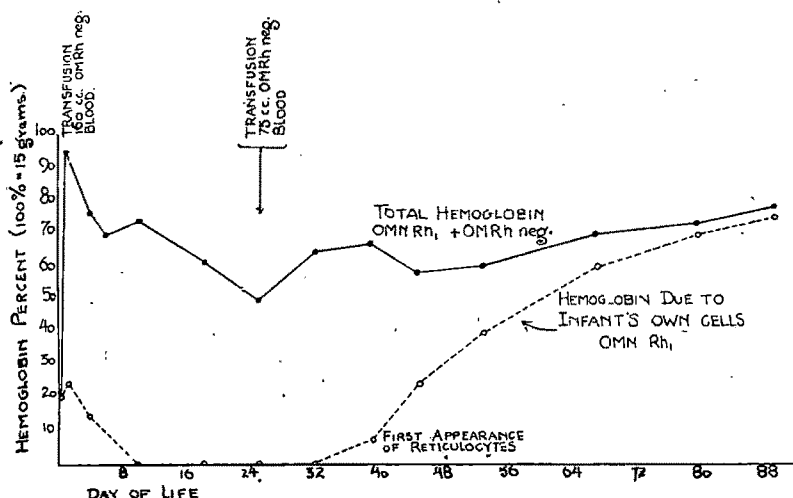
mined at this time and was found to be only 50 per cent; this indicates that before the transfusion it must have been less than 20 per cent. An additional 80 cc. of blood followed by 5 cc. of 10 per cent solution of calcium gluconate was injected (to counteract the relatively large amount of citrate given). The infant when sent to the nursery was in excellent condition.

Grouping tests on blood obtained from the umbilical cord showed that the infant's blood belonged to group O, type MN and type Rh.

The infant's subsequent course was interesting. Considering that the baby weighed 8 pounds and 3 ounces (3,714 Gm.) and therefore had a blood volume of approximately 240 to 250 cc., the 160 cc. of Rh-negative blood transfused would be expected to maintain her hemoglobin level at about 60 to 65 per cent, even if all her own blood cells were destroyed. During the first twenty-four hours the hemoglobin level actually ranged between 90 and 100 per cent. Within forty-eight hours the hemoglobin had dropped to 77 per cent; it was still above 70 per cent when the infant was discharged on the tenth day. The infant was followed

seen that the initial drop in hemoglobin which occurred in the hospital was due to the elimination of the last remnants of the infant's own cell and that for a period of a month the only blood detectable in the infant's circulation was that received from the donor. Then, finally, the differential agglutination test revealed the reappearance of the patient's own type of blood gradually replacing the donor's erythrocytes as they disappeared from the circulation. (Currently, reticulocytes made their appearance on the blood smears.) It was not until more than two months after the last transfusion that all of the donor's blood had been eliminated from the infant's body.

The question arises why there was no trace of the patient's own blood in her circulation for as long a period as one month. It may be that



Results of differential agglutination tests in case 3.

up at home, where it was observed that her gain in weight was poor and that progressive pallor developed. When she was 1 month old, her hemoglobin had dropped to 50 per cent, and it was necessary to give another transfusion of 75 cc. of Rh-negative blood. After the transfusion the hemoglobin rose to 67 per cent. The hemoglobin then fell slightly, but within a short time it rose again. At the time of writing the infant was 3 months old and thriving, her hemoglobin being above 75 per cent.

The results of the differential agglutination tests¹¹ were illuminating (see chart). On the first day, after the initial transfusion of 160 cc. of Rh-negative blood had been given, three fourths of the 95 per cent hemoglobin could be attributed to the donor's blood and only one fourth to the patient's own blood. It will be

the anti-Rh isoantibodies of the mother had damaged the erythropoietic tissue of the infant so that transient aplastic anemia developed in the latter. Or perhaps the infant's body contained an excess of Rh isoantibodies which destroyed her Rh-positive blood as quickly as it was released into the circulation, this process continuing until all the Rh isoantibodies were exhausted. In either event the transfusions tideed the infant over until its own blood became available to the circulation.

As has already been mentioned, no anti-Rh agglutinins had been found in the mother's blood before delivery, but studies of the maternal serum after the cesarean operation yielded interesting results.¹² A sample of serum obtained one week after delivery revealed the presence of anti-Rh agglutinins of high titer (128). However, one month later agglutinins were no longer

11. For a description of the technic see Wiener, A. S.: Hemolytic Transfusion Reactions: I. Diagnosis with Special Reference to the Method of Differential Agglutination, *Am. J. Clin. Path.* **12**:1889 (April) 1942.

12. These are presented in detail elsewhere.⁴

emonstrable in the serum. Tests of the serum obtained at this time showed that it contained anti-Rh blocking antibodies, the titer of these being between 2 and 4. It is interesting to speculate whether the evanescent appearance of potent anti-Rh agglutinins in our patient's serum was the result of the provocative dose of Rh-positive blood given in the biologic test.

CASE 4.—Obstetric History.—This patient, who was pregnant for the fourth time and was near term when first seen, gave the following obstetric history:

First pregnancy, normal full term male, who is now years old.

Second pregnancy, miscarriage at ten weeks.

Third pregnancy (a few years before the present one), erythroblastic infant who died after four days.

Results of Grouping Tests.—Grouping tests of the parents and of the surviving child showed:

Blood of	Group and Subgroup	MN Type	Rh Type
Father	A ₂ B	MN	Rh ₁ Rh ₂
Mother	A ₁	MN	Negative
son (9 years old)	A ₁	M	Rh ₂

Prognosis.—In spite of the fact that no anti-Rh agglutinins could be demonstrated in the maternal serum, these serologic findings supported the diagnosis of erythroblastosis in the last child. Although the first child's blood was Rh positive, he had escaped, probably because a sufficient degree of sensitivity had not developed during the period of gestation. Since the husband's blood belonged to type Rh₁Rh₂, it was to be expected that every child would have Rh-positive blood and would be subject to the disease.

Procedure.—When the patient reached term and went into labor, preparations were made to give the expected infant an exsanguination transfusion as soon as it was born. From the parents' blood groups, it was clear that the expected child had to have blood of group A, B or AB and could not have group O blood. Arrangements were made to have Rh-negative donors of these three groups at hand. The patient delivered an 8 pound (3,629 Gm.) female infant, who appeared robust and normal except for a slight bronzing of the skin. Blood was taken from the umbilical cord, and while it was being tested in the laboratory a biologic test was performed on the mother. Fifty cubic centimeters of blood of group A, type Rh₁Rh₂ was injected intravenously. Within thirty-five minutes a severe chill developed, which was followed by a rise in temperature. Blood drawn during the chill showed the presence of hemoglobinemia, which proved that the mother was indeed sensitive to the Rh factor. In the meantime, grouping tests on the blood from the cord showed that the infant's blood belonged to group A and was Rh positive. (Subsequent tests proved that the blood of the infant belonged to group A, type N and type Rh₂. Smears of the blood from the cord stained later showed numerous erythroblasts in every field, and the cord serum had an icterus index of 45. There was no evidence of anemia, however.) In view of the mother's positive reaction to the biologic test and the finding that the infant's blood was Rh positive, blood was drawn from the donor with group A, Rh-negative blood. Fifty cubic centimeters of this blood was transfused to the infant through an incision into the internal sphenous vein. An attempt to withdraw blood through the umbilical cord was unsuccessful because the vessels had already become thrombosed and did not bleed even

when cut in several places. By various avenues, namely, the anterior fontanel and both deep femoral veins, a total of only 50 cc. of the infant's blood could be withdrawn. An additional 70 cc. of the donor's blood was then administered. While at first we had planned to carry out a complete exsanguination transfusion, the procedure was discontinued at this point because of the difficulties encountered and the fact that the infant looked so well that no further treatment seemed necessary.¹³

Course.—For the first three days after birth the baby appeared perfectly well, and the hemoglobin ranged from 95 to 100 per cent, with the red blood count averaging about 5,000,000. The only disturbing factor was the persistence of icterus. On examination of the urine, no bile was found, indicating that the bile was not being excreted by that route. (In comparable cases previously observed, the urine was usually deeply bile stained, the elimination of bile being accompanied by clearing of the clinical jaundice.) On the evening of the third day there was a slight rise in temperature; the infant became lethargic and refused his feeding. Splenomegaly and hepatomegaly were present, and on the morning of the fifth day the infant died. A sample of blood obtained before death had an icterus index of only 22. In an autopsy performed by Dr. David M. Grayzel enlargement of the liver and of the spleen, generalized icterus and kernicterus were the principal gross abnormalities noted.

A sample of the mother's blood obtained about a month after delivery showed anti-Rh agglutinins with a titer of 16.

This case demonstrates that blood transfusion is not the complete answer to the problem of the treatment of hemolytic anemia of the newborn, even when the infants appear to be in good condition at birth. Transfusions are merely a substitution therapy, and therefore save only those infants who would otherwise die from the extreme anemia brought about by the destructive action of the maternal isoantibodies. Hemolytic anemia is not, however, the sole mechanism of death in this disease. Some infants will not suffer a marked drop in the amount of hemoglobin but still may succumb to the lethal effects of retaining the products of hemolysis in their bodies, and a few die of hemorrhagic diathesis, which does not appear to be influenced by simple transfusion of Rh-negative blood or by administration of vitamin K. It is theoretically possible that when an infant's blood is susceptible to the action of Rh antibodies a complete exsanguination transfusion, entailing the removal of all but a small quantity of the infant's blood and its replacement by Rh-negative blood at

13. In a subsequent experiment, performed on a premature mongolian idiot weighing only 4 pounds (1,814 Gm.), we were able to effect a 90 per cent substitution of the infant's blood with donor's blood (as proved by differential agglutination tests). To accomplish this, it was necessary to withdraw as much as 275 cc. of blood from the infant and concurrently to inject a like amount of donor's blood, although the calculated blood volume of the infant was only 150 cc.

birth or as soon thereafter as possible may serve to prevent a lethal outcome. One must keep in mind when treating such infants that occasionally mental deficiency (as a result of kernicterus) or cirrhosis of the liver¹⁴ may remain as a sequelae after the immediate threat to life has been overcome by blood transfusion. Fortunately all of the infants whose lives we have saved by blood transfusion (10 in number¹⁵) have developed into apparently normal children.

A question which remains unanswered is why some infants with a severe degree of hemolysis have deep jaundice which clears within a few days without any harmful after-effects, while in others with a lesser degree of hemolysis and with slight jaundice the icterus persists to the detriment of the patient. As is suggested in our case report, excretion of bile by the kidneys appears to be an important factor. A second factor, more difficult to assess, may be the efficiency of the liver in the elimination of bile. Further study of this problem is urgently needed.

COMMENT

The final proof or disproof of intragroup sensitivity is the result of the biologic test. This is true not only in the more common case in which the patient's blood is Rh negative, but also in the rarer one involving a patient with Rh-positive blood.

The two principal applications of the biologic test are: (1) as a precautionary measure before blood transfusions and (2) as a means of detecting isoimmunization in pregnancy, for example, in pregnancies resulting in stillbirths or miscarriages the cause of which is obscure. The first 2 cases of the present paper illustrate the second application. In case 2 it was proved that the stillbirths were caused by sensitivity to the Rh factor; in fact, the patient's reaction to the test dose of 50 cc. of Rh-positive blood was so violent that we now are hesitant about applying the test again merely as a routine diagnostic procedure. The recent discovery of the blocking Rh antibodies fortunately makes possible a relatively simple in vitro test for Rh sensitivity which largely does away with the need for the biologic test in such cases. The main field of usefulness for the biologic test is,

we feel, as a preliminary to blood transfusion particularly post partum.

In emergencies such as severe postpartum hemorrhage or shock following a cesarean operation the possibility of Rh isoimmunization by the fetus must always be borne in mind; so we have adopted the following procedure in order to expedite transfusions to such a patient: A sample of the patient's blood is drawn and sent to the laboratory for tests of blood grouping and of the Rh factor. Through the same needle 50 cc. of group O blood from an intern or a nurse is injected (this is usually and preferably Rh positive). Without the needle's being withdrawn from the vein infusion of plasma or of isotonic solution of sodium chloride is started. This infusion will not interfere with the results of the biologic test and will maintain the patient's blood pressure during the hour that one must wait for the result of the test. After one to one and one half hours, a second sample of blood is obtained and the serum or plasma separated from this sample is compared with the first serum. If the result of the test is negative the patient may be given any amount of blood from the same donor. If Rh-positive blood was used for the test, the Rh type of any additional donors may be disregarded. A negative result of the biologic test obtained in this way from a patient with Rh-negative blood leaves the transfusionist free to use blood of any compatible group, Rh positive as well as Rh negative, without danger of a transfusion reaction caused by Rh incompatibility. Were no information available other than the fact that the patient's blood is Rh negative, only Rh-negative blood could be used for such transfusions, a requirement which would sharply limit the choice of donors. This consideration is of some importance in these cases since as much as a liter or even 2 liters of blood or more is required in many cases of postpartum hemorrhage. Patients with Rh-positive blood will hardly ever offer any problems in the selection of donors.

The procedure outlined for transfusion to a postpartum patient has the advantage that no time is lost. While waiting for the results of the serologic test the patient is receiving plasma or saline solution, and by the time the hour of past grouping and Rh tests will have been completed and enough information will be on hand for safe conduct of further transfusion. Incidentally, the direct in vitro matching test for Rh sensitivity is not entirely reliable.

With regard to the therapy of the infant in case 3 is probably the most dramatic thus far reported as an example of the life-saving value

14. Parsons, L. G.: Haemolytic Disease of the Newborn, *Correspondence, Brit. M. J.* 1:371 (March 11) 1944.

15. Wiener, A. S., and Wexler, I. B., Transfusion Therapy of Acute Hemolytic Anemia of the Newborn, *Am. J. Clin. Path.* 13:393 (Aug.) 1943. Wiener, A. S.: The Role of the Subtypes of Rh in Hemolytic Transfusion Reactions and in Erythroblastosis, *ibid.* 14:52 (Jan.) 1944.

of Rh-negative blood. In fact, if the donor's blood had not been drawn before the infant was born, ready to be administered at a moment's notice, the infant's life would probably have been lost, since it is doubtful that she could have survived more than half an hour after birth. It seems probable that in view of the low hemoglobin content of the infant's blood and the continuation of hemolysis she would have been still-born had the cesarean section been performed one day later. However, we do not consider this case an argument in favor of early cesarean section. Such procedure would increase the hazard of the childbirth for the mother and also for the infant on account of prematurity, and neither of these disadvantages is balanced by the remote chance of saving the infant from the action of the maternal isoantibodies. We do feel, that when a woman with Rh-negative blood gives a history of having had an erythroblastotic baby and the serologic tests indicate that the child about to be born will have Rh-positive blood and therefore be subject to hemolytic disease, preparations for transfusion immediately after birth are indicated.

SUMMARY

The biologic test was employed for the detection of sensitivity to the Rh factor. In a woman who had previously had repeated miscarriages, a negative biologic reaction proved that these were not caused by Rh sensitivity, even though her blood was Rh negative and her husband's was Rh positive. On the other hand, in a case involving a husband with Rh-positive blood and a wife with Rh-negative blood, who had had two stillbirths of obscure cause, a positive biologic test proved that isoimmunization was responsible, even though in vitro tests for anti-Rh agglutinins in the woman's serum had previously given negative results.

Two cases of hemolytic disease of the newborn are described in which the patients were treated by transfusions of Rh-negative blood. In 1 case the therapy was dramatically life-saving, while in the second, in which the disease was apparently milder, the infant died of cholemia and kernicterus.

64 Rutland Road.
1672 Ocean Avenue.
910 Park Place.

Case Reports

ABSCESSSES OF THE LUNG IN A PREMATURE BABY

WILLIAM LEACH, M.D., AND MARK HOLLAND, M.D.

SHENANDOAH, PA.

MAHANOTY CITY, PA.

Pulmonary abscess undoubtedly occurs much more frequently in children than is commonly supposed, but it is frequently missed because it is difficult to detect it in children and especially in infants. Baron¹ in 1908 reported an instance of abscess of the lung complicating otitis media in a child 2 weeks of age. He was able to collect from the literature 7 other cases of pulmonary abscess in infants. In the other 7 cases the diagnosis was not made ante mortem, whereas in his case the diagnosis was made after aspiration of the lung. Lilienthal² reported a successful operation on a patient three weeks after birth, and Struthers³ reported an instance of pulmonary abscess in a boy aged 24 days.

The most important causes of pulmonary abscess in children are antecedent pulmonary infections and operations, especially tonsillectomies. Authorities disagree as to the incidence of pulmonary abscess following tonsillectomy. According to Moore⁴ the incidence is 1 instance of pulmonary abscess per 3,000 tonsillectomies, whereas Keiper⁵ stated that pulmonary abscess occurs once in every 730 tonsillectomies. The variation in the reports from different clinics is probably due to differences in technic. The relative frequency of post-tonsillectomy pulmonary abscess is not realized by a good many otolaryngologists because frequently the patient does not return to the physician who removed the tonsils, but consults the family physician, who may or may not consider the relationship between the tonsillectomy and the pulmonary symptoms which follow it.

A large number of micro-organisms have been obtained from pulmonary abscesses in children. Smith⁶ expressed the view that 75 per cent of the bacterial abscesses and 50 per cent of abscesses in children are due to staphylococci. In a series of 16 cases from the Graham Clinic, Ermatinger⁷ found hemolytic *Staphylococcus aureus* in 80 per cent. In other cases reported many other organisms have been found, such as *hemolyticus viridans* and nonhemolytic streptococci, *Micrococcus catarrhalis*, influenza bacilli and others. Rarely pneumococci may be the cause of pulmonary abscess in children. (Recently has the importance of Vincent's organisms in the production of abscess of the lung been recognized, although the association has long been known.)

The location of pulmonary abscesses varies in the different groups studied. Singer and Graham⁸ in a study of 34 cases found 85 per cent of the abscesses in the right lung and 15 per cent in the lower lobe of the right lung. Clerf,⁹ in studying a series of 77 persons of all ages with abscess of the lung who were examined bronchoscopically, found the right lung involved in 62 per cent and the left lung in 28 per cent. The predominance of involvement of the lower lobe of the right lung in pulmonary abscess following aspiration of foreign bodies is undoubtedly due to the more direct continuation of the right main bronchus of the trachea.

The symptoms and signs of pulmonary abscess in infants and children are not so characteristic as in adults, and hence diagnosis is more difficult. The chief source of difficulty is that in children, especially younger ones, seldom if ever expectorate the characteristic sputum which is so frequently of importance in the diagnosis.

1. Baron, L.: Ueber Lungenabscesse bei Säuglingen, *Berl. klin. Wchnschr.* **45**:98, 1908.

2. Lilienthal, H.: Lung Abscess and Empyema in a Child Six Weeks Old, *S. Clin. North America* **10**:451, 1930.

3. Struthers, R. R.: Abscess of Lung: Report of Case in Infant Twenty-Four Days of Age, *Canad. M. A. J.* **16**:168, 1926.

4. Moore, W. F.: Pulmonary Abscess: Analysis of 202 Cases Following Operative Work About the Upper Respiratory Tract, *J. A. M. A.* **78**:1279 (April 29) 1922.

5. Keiper, G. F.: The Tonsil Question Up to Date, *Laryngoscope* **31**:777, 1921.

6. Smith, D. T.: Diagnosis and Treatment of Pulmonary Abscess in Children, *J. A. M. A.* **103** (Sept. 29) 1934.

7. Ermatinger, L. H.: Microorganisms of Pulmonary Abscess and Bronchiectasis, *J. Infect. Dis.* **43**:391, 1932.

8. Singer, J. J., and Graham, E. A.: A Study of Thirty-Four Cases of Abscess of the Lung, *J. A. M. A.* **81**:193 (July 21) 1923.

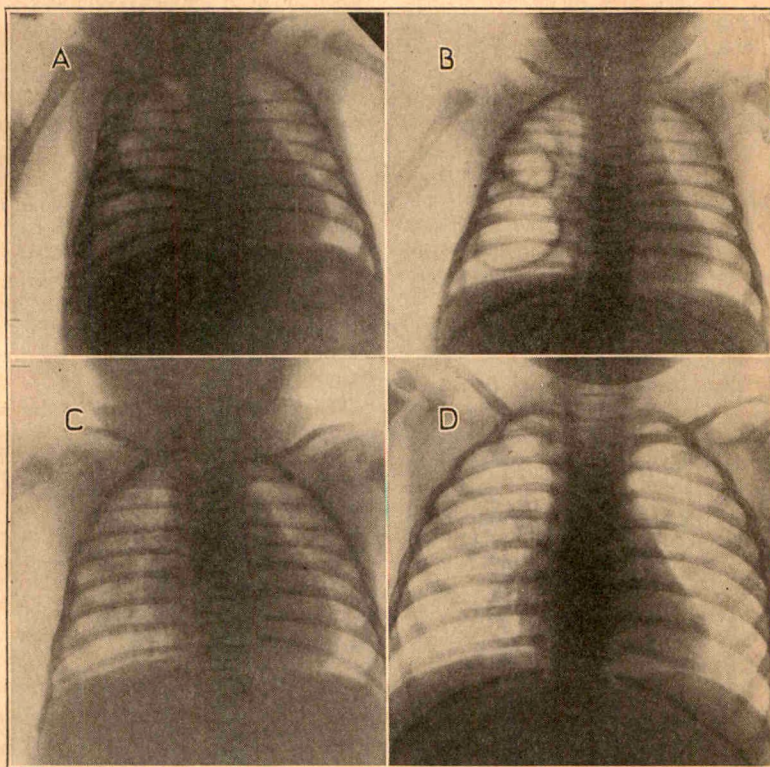
9. Clerf, L. H.: Pulmonary Abscess Following Tonsillectomy: Bronchoscopic Considerations, *J. Otolaryng.* **11**:192 (Feb.) 1930.

pulmonary abscess. The physical signs, especially in children and infants, are relatively few. Pallor and anemia are early manifestations. A diminished percussion note is the most important thoracic sign. Pulmonary dulness may be the only evidence of abscess, the signs being those of pneumonia or consolidation of the lobe rather than of cavitation. Limitation of motion on the affected side is likely to occur in young children. The usual signs of cavitation, such as crackpot percussion note and amphoric breathing, are usually not found in children. In most instances leukocytosis is present: The count

REPORT OF A CASE

The baby (M. R.), a girl, was born Jan. 3, 1942, six weeks prematurely, and weighed 5 pounds (2,268 Gm.) at birth; the delivery was normal. The baby was given a mixture of evaporated milk, water and corn syrup and seemed to be taking this diet fairly well and to be thriving.

On March 19, 1942, at the age of 10 weeks, the baby was seen by one of us (M. H.). She had had an intermittent fever for about one week and had a non-productive cough. At this time her temperature was 101 F.; slight dulness to percussion and decreased breath sounds were noted over the right side of the chest. Fine crepitant rales were heard in the right axilla. Administration of sulfathiazole (8 grains [0.52 Gm.] daily) was started. On March 20 the baby's



Roentgenograms of the chest taken March 28 (A), April 19 (B), June 23 (C) and December 27 (D).

may be as high as 30,000 to 40,000. Because the physical findings are frequently of little value, roentgenograms are particularly valuable in the diagnosis of pulmonary abscess in young children. In infants, because of the early extension of the process to the pleura with the development of empyema, the primary condition is likely to be overlooked. Pulmonary abscess should be suspected in all cases of empyema in children, although empyema occurs more frequently than pulmonary abscess.

We had the opportunity of seeing a 10 week old premature baby who had three abscesses in the right lung.

temperature was 101.2 F., the cough had increased a little in frequency and again the breath sounds were decreased over the right side of the chest. On March 22 the baby had an attack of coughing that lasted for about twenty minutes. The cough was short and irritative, and it was so frequent that the baby had to be held by the mother, as at times she could not get her breath; nothing seemed to be able to relieve the coughing spasm. At this time the dulness was marked over the right side of the chest, and the breath sounds were much decreased.

Because of the severe coughing spasm and the physical findings the baby was taken to Locust Mountain Hospital, Shenandoah, Pa., and there the chest was aspirated by one of us (W. L.). The needle was inserted in the right side of the chest at about the posterior axillary line, and 20 cc. of thick, creamy pus was removed. On culture it was found to contain staphylococci. After

the aspiration the cough stopped, and the baby seemed to be in fairly good condition.

On March 24 her temperature was 98 F. in the morning; it rose to 101 F. in the latter part of the afternoon and was down to 98 F. again at midnight; there was no cough, but the dulness and the decreased breath sounds were still present over the right side of the chest.

On March 28 another coughing spasm similar to the one on March 22 occurred, and again the baby coughed persistently for about fifteen minutes without any relief. The chest was then aspirated for the second time, and 30 cc. of creamy pus was obtained, which seemed thicker in consistency than that aspirated previously. The blood count on March 28 showed: hemoglobin 56 per cent, red blood cells 2,240,000 and white blood cells 14,900 with polymorphonuclears 66 per cent, lymphocytes 33 per cent and eosinophils 1 per cent. Administration of sulfathiazole was discontinued on this date. A roentgenogram made on March 28, after the second aspiration, was described by the roentgenologist as follows (fig. A): "The right side of the chest presents a rather unusual appearance. There is apparently little if any accumulated fluid or pus present. But the entire right side of the chest appears as three large cavities—one, the largest, occupying the lower half of the right side of the chest and two smaller cavities occupying its upper half. All three are surrounded by a rather dense wall. The left lung is clear."

On March 30, two days after the second aspiration, the temperature was still normal. The baby was coughing slightly, and there was still dulness with decreased breath sounds in the right side of the chest. The child looked better and was taking her formula well, supplemented with 25 mg. of ascorbic acid and 10 drops of percomorph liver oil daily and $\frac{1}{2}$ teaspoon of an elixir of ferrous sulfate twice a day. At this time she weighed 8 pounds 10 ounces (3,912 Gm.). The baby continued to do well.

On April 19 a second roentgenogram was taken (fig. B), which was described as follows: "There is no evidence of fluid or pus in the right pleural cavity at this time, but the three large cavities are still present in the right side of the chest. The cavities, however, are not nearly as large as on the first examination."

The blood count on this date showed hemoglobin 7 per cent, red cells 3,160,000 and white cells 6,650, with polymorphonuclears 16 per cent and lymphocytes 8 per cent. The temperature had been between 98 and 99 F., and the breath sounds in the right side of the chest were coming through better than before, but they were still somewhat decreased.

On June 23 another roentgenogram of the chest was made (fig. C), which showed the following picture: "The cavities that were present in the right side of the chest have now almost completely disappeared, and most of that side of the chest seems to be filled with what appears to be normal lung structure. The shadow of the heart is considerably above the average in size for a person of this age, and there is considerable widening of the shadow of the mediastinum." On August 2, when the baby was 8 months of age, she appeared to be in good health. Her weight was 15 pounds 1 ounce (6,832.23 Gm.), and her height was 27½ inches (69 cm.). She was very active, took feedings well and was not having any respiratory difficulties. On physical examination there was still a slight decrease in breath sounds, especially in the right axilla; the borders of the heart still were somewhat enlarged. The baby continued to do well.

On December 27 a final roentgenogram was taken (fig. D), on which the following report was made: "Reexamination of the chest shows some accentuation of the peribronchial markings in the medial portion of each lung, more especially the right. The apexes and the peripheral pulmonary fields appear clear. The costophrenic angles are well outlined, the diaphragm is smooth and the heart and the mediastinum appear normal."

The roentgenologist did not mention the previous cavities, which had undoubtedly disappeared by this time. It was also noted that the heart did not show any enlargement in the last picture. Since then the child has been normal.

SUMMARY

Abscesses of the lung developed in a 10 week old baby who had been born six weeks prematurely.

Locust Mountain State Hospital.
27 South Catawissa Street.

HEMOLYTIC ANEMIA IN INFANCY

REPORT OF A CASE WITH DEMONSTRATION OF HEMOLYTIC ACTIVITY OF SERUM

J. K. DAVID JR., M.D.,

AND

A. S. MINOT, Ph.D.

NASHVILLE, TENN.

Recently a case of recurrent acute hemolytic anemia in a 4½ month old infant was observed in the pediatric service of Vanderbilt University Hospital.¹ During a hemolytic crisis it was possible to demonstrate hemolytic activity of the patient's serum against his own red blood cells as well as against those of another patient of the same blood group. After splenectomy the patient made a complete recovery. This was associated with disappearance of the hemolytic activity of his blood serum.

During infancy recurrent hemolytic anemia, accompanied by slight icterus and enlargement of the spleen, is uncommon. In pediatric literature this condition has been classified as a form of the disease which is variously referred to as congenital hemolytic icterus, congenital hemolytic anemia and familial spherocytosis. However, the usual criteria by which a diagnosis of congenital hemolytic anemia is established may not all be present in the infant. In addition, the clinical course is not the one usually seen in the adult.

Rarely is a history of similar disease in other members of the family obtained when the disease is encountered in the first year of life. The characteristics of the disease as it occurs in infancy have been well summarized by Abt² and by Diamond.³ The initial manifestation of the disease often takes the form of an acute hemolytic crisis. Severe anemia may develop suddenly. In the infant icterus is usually slight, even during the acute hemolytic crisis, pallor and splenomegaly being the most outstanding physical findings.

Because of the lability of the infantile hemopoietic system, the changes in the peripheral blood picture are usually more striking in the infant than in the adult. The response of the reticulocytes during a hemolytic crisis may be

very great, and these cells may comprise the majority of the circulating erythrocytes. Nucleated red blood cells are also regularly seen in the peripheral blood during the acute hemolytic crisis. Increased fragility of the erythrocytes to hypotonic solution of sodium chloride, which is usually considered diagnostic of the condition, may not be present in the infant. Evidence of increased destruction of blood is uniformly present. There is elevation of the level of serum bilirubin and increase in the excretion of urobilin in the feces.

Results following splenectomy are good in the great majority of cases. Because of the rapidity with which profound anemia may develop during an acute hemolytic crisis, it may be disastrous to postpone splenectomy too long. After preparation of the patient with transfusions of blood the operation should be performed. After splenectomy evidence of excessive destruction of blood usually disappears, and the level of hemoglobin and the erythrocyte count gradually rise to normal values.

REPORT OF A CASE

A 4½ month old white boy was first admitted to the pediatric service on Sept. 27, 1943, because of pallor and irritability of twenty-four hours' duration. The child's history was interesting in that he had had considerable vomiting and diarrhea during the first three months of life. However, during the month prior to his admission he had had good health and had gained weight satisfactorily. The parents had noted no icterus or pallor in the infant during the neonatal period. No history of jaundice or anemia in any other member of the family could be elicited. One sibling, 4 years old, was living and well. Twenty-four hours before his admission the patient became pale and listless and refused his feedings.

Physical examination revealed a well developed and well nourished infant. He appeared listless and breathed rather rapidly. The skin and the mucous membranes were extremely pale, and the scleras were slightly icteric. The heart was enlarged, and a blowing systolic murmur was audible over the entire precordium. There was slight injection of the nasal and pharyngeal mucosae. The spleen was easily palpable 2 cm. below the costal margin. The results of the remainder of the physical examination were not remarkable.

Laboratory tests furnished the following data: hemoglobin 4.5 Gm. per hundred cubic centimeters of blood, red blood cell count 2,300,000 and white blood cell count 20,000. The differential count showed segmented

From the Department of Pediatrics, Vanderbilt University School of Medicine.

1. Dr. James C. Overall permitted us to report this case.

2. Abt, A. F.: Hemolytic Disease in Infants, *Am. J. Dis. Child.* **60**:812 (Oct.) 1940.

3. Diamond, L. K.: *M. Clin. North America* **21**: 401, 1937.

polymorphonuclear leukocytes 36 per cent, stab forms 8 per cent, juvenile forms 6 per cent, eosinophils 1 per cent, basophils 1 per cent, lymphocytes 45 per cent and myelocytes 3 per cent. Eighteen nucleated red blood cells were counted per hundred white blood cells. The icteric index was 15 and the van den Bergh reaction indirect. The reaction to the Kahn test of the blood was negative.

The patient was thought to have acute hemolytic anemia secondary to an infection of the upper part of the respiratory tract. He was given transfusions of whole blood. No difficulty was experienced in cross matching the blood, and no untoward reaction followed transfusion. His condition improved rapidly, and he was discharged on Oct. 1, 1943. At this time his hemoglobin was 10.2 Gm. per hundred cubic centimeters of blood, and his red blood count was 4,000,000.

Five days later the child was readmitted to the hospital because of the sudden onset of dyspnea, drowsiness and pallor thirty-six hours before admission. Physical examination at this time gave virtually the same results as on the preceding admission. The skin and the mucous membranes were very pale and slightly icteric. The spleen was palpable 4 cm. below the costal margin. Laboratory analysis showed hemoglobin 4.3 Gm., red blood cell count 1,400,000 and white blood cell count 32,000. There were 6 nucleated red blood cells per hundred leukocytes. Thirty-two per cent of the erythrocytes were reticulocytes. There was no increase in the erythrocyte fragility to hypotonic solution of sodium chloride. The patient's red blood cells showed hemolysis beginning with a concentration of 0.42 per cent and complete at 0.34 per cent. Hemolysis of the control cells began at 0.40 per cent and was complete at 0.32 per cent. Sickie cell preparations showed no sickling of the patient's red cells at the end of twenty-four hours. Fragility test on both parents gave normal results.

Again the child was treated with repeated transfusions of whole blood. His general condition improved rapidly, and he was discharged on Oct. 13, 1943. At this time his hemoglobin was 11 Gm. per hundred cubic centimeters, and his red blood cell count was 3,300,000.

Two days later the child was admitted for the third time. Eighteen hours before admission he had again become drowsy, pale and dyspneic. Physical examination again revealed marked pallor, slight icterus and splenomegaly. There had been a precipitous drop in the hemoglobin to 4.0 Gm., and the erythrocyte count had fallen to 1,200,000. Fragility tests again showed normal resistance of the erythrocytes to hypotonic solution of sodium chloride. Blood serum and cells were obtained at the time of admission, and an attempt was made to demonstrate hemolytic activity of the patient's serum against his own cells as well as against cells of another person of the same blood group. The results of these tests will be discussed under experimental procedure.

The patient was given repeated transfusions of whole blood. After this the hemoglobin rose to 11 Gm. and the red cell count to 4,200,000. However, forty-eight hours later the hemoglobin had dropped to 4.3 Gm. and the erythrocyte count to 1,600,000. The child was given three more transfusions, totaling 300 cc. In spite of this there was only a slight rise in the level of hemoglobin, to 6.4 Gm., and in the erythrocyte count, to 2,200,000.

Because of the recurrent, acute hemolytic crises and the failure of the patient to respond to blood transfusions except for brief periods, splenectomy was performed on Oct. 18, 1943. The infant stood the operative procedure well.

The spleen weighed 122 Gm. It was deep reddish purple. Microscopic examination revealed some thick-

ening of the capsule. The sinuses were engorged with red blood cells, hemosiderin and occasional polymorphonuclear cells. There was little fibrosis, and the lymphoid tissue appeared normal.

The patient's postoperative course was uneventful. There was no further evidence of destruction of blood during his stay in the hospital. Examination of his blood three months later showed hemoglobin 14 Gm and red blood cell count 4,500,000.

EXPERIMENTAL STUDIES

Method.—Estimation of the hemoglobin content of the serum may serve as an index of destruction of blood in certain cases of hemolytic anemia. The value of the serum hemoglobin in blood obtained under carefully controlled conditions will be determined by three factors: The rapidity with which the destruction of red blood cells proceeds, the rate at which hemoglobin in the serum is converted into bile pigments, and the rate of excretion of hemoglobin in the urine.

Determinations were made of the hemoglobin in the patient's blood plasma and in several samples of blood plasma obtained from normal persons. In obtaining the plasma the precautions against hemolysis outlined by Ham⁴ were observed. The hemoglobin content was determined by the colorimetric benzidine method described by Wu⁵ as modified by Bing and Baker.⁶ Our results on normal plasma, which are in agreement with the values reported by Ham, ranged from 2 to 5 mg. of hemoglobin per hundred cubic centimeters of plasma. On two occasions before splenectomy the patient had plasma hemoglobin contents of 34 and 47.5 mg. respectively per hundred cubic centimeters. After splenectomy the plasma hemoglobin was 6.6 mg per hundred cubic centimeters of plasma.

Blood serum and a 10 per cent suspension of washed red blood cells were prepared from the blood of the patient and from that of a control of the same blood group. Two series of tests were then set up as follows: In series A, 0.5 cc. of the suspension of the patient's cells was added to 0.5 cc. portions of (a) the patient's serum, (b) the acidified serum of the patient,⁷ (c) the control's serum and (d) the acidified serum of the control. In series B, 0.5 cc. of the control cell suspension was set up in the same manner, with the two serums at both normal and reduced *pH*. After gentle mixing the tubes were incubated for an hour at 37 C. and then centrifuged. The supernatant serum was carefully removed. The degree of hemolysis in the various tubes was measured by doing quantitative hemoglobin determinations on this serum. The total value of hemoglobin determined was corrected by subtracting the amount of hemoglobin which was present in the respective serums before the cell suspensions were added. Thus the figures for hemoglobin presented here show the increment in serum hemoglobin due to hemolysis during the period of incubation.

4. Ham, T. H.: Studies on Destruction of Red Blood Cells: Chronic Hemolytic Anemia with Paroxysmal Nocturnal Hemoglobinuria, *Arch. Int. Med.* **64**: 1271 (Dec.) 1939.

5. Wu, H.: *J. Biochem.* **2**:189, 1922-1923.

6. Bing, F. C., and Baker, R. W.: *J. Biol. Chem.* **92**:589, 1931.

7. The acidified serum was prepared according to the directions of Ham by the addition of 5 per cent (by volume) of third-normal hydrochloric acid to the serum.

Results.—The table shows the results of studies carried out before and after splenectomy was performed on our patient. These results indicate an abnormal hemolytic activity of the patient's serum against his own red blood cells as well as against red blood cells from a normal control of the same blood group. This hemolytic activity was enhanced by acidification of the serum. Incubation of the patient's red blood cells with normal serum, at either normal or reduced p_H , showed only the same slight degree of hemolysis as was observed when normal cells were incubated under similar conditions. The patient's serum, however, caused about four times as much hemolysis of both the patient's and the control's cells as did normal serum. Acidification of the patient's serum increased the hemolytic effect on

Attempts to demonstrate serum hemolysins in patients with the disease have so far as we know been uniformly unsuccessful. Bergenhem and Fåhræus⁹ suggested that the disease may be due to an increased production of lysolecithin, a hemolytic substance present in normal blood. Singer¹⁰ found no evidence of increased production of lysolecithin in patients with congenital hemolytic anemia.

The findings in the present case would exclude a mechanism such as that encountered in paroxysmal nocturnal hemoglobinuria. In that disease increased hemolysis of erythrocytes occurs when the cells are incubated at a decreased p_H in the presence of normal serum. The defect in cases of that disorder is apparently in the erythrocytes: It consists of decreased resistance by the cells to a reduced p_H in the presence of some substance normally present in all serum.

Our findings are more nearly analogous to those described in certain cases of acute acquired hemolytic anemia in which hemolysins have been demonstrated.¹¹ Unfortunately, attempts to determine the specific nature of the hemolytic substance in the present patient's serum were not made.

One may well question the justifiableness of classifying this case and similar cases with cases of congenital hemolytic anemia. The criteria for the diagnosis of that condition should probably include the presence of spherocytosis in other members of the family and the persistence of spherocytosis and of increased hypotonic fragility of the red cells after splenectomy. It is our plan to test patients with familial hemolytic icterus for hemolytic activity by the method outlined here. The demonstration of hemolysins in cases with a positive family history of the disease as well as in cases like the one here presented would suggest a common mechanism.

Increments in Serum Hemoglobin of a Patient with Recurrent Acute Hemolytic Anemia Before and After Splenectomy

Before Splenectomy		Increments in Serum Hemoglobin, Mg.
A. Patient's cells	+ Patient's serum.....	50.6
	+ Acidified patient's serum	82.6
	+ Control's serum.....	12.6
	+ Acidified control's serum	12.6
B. Control's cells	+ Patient's serum.....	47.0
	+ Acidified patient's serum	111.0
	+ Control's serum.....	9.2
	+ Acidified control's serum	9.1
After Splenectomy		
A. Patient's cells	+ Patient's serum.....	3.0
	+ Acidified patient's serum	7.0
	+ Control's serum.....	3.1
	+ Acidified control's serum	3.1
B. Control's cells	+ Patient's serum.....	4.4
	+ Acidified patient's serum	3.7
	+ Control's serum.....	2.1
	+ Acidified control's serum	3.7

both the patient's and the control's cells. After splenectomy, the hemolytic activity of the patient's serum was no longer present.

COMMENT

Attempts to determine the pathogenetic mechanism in congenital hemolytic anemia have so far been unsuccessful. Most observers have considered the abnormality to be the production by the bone marrow of a defective erythrocyte, the spherocyte, which is less resistant to hypotonic solution of sodium chloride than is the normal red blood cell. However, a number of cases of the disease have been reported in which there was normal fragility of the erythrocytes.⁸

8. Schiff, E.: Arch. Dis. Childhood **13**:264, 1938.
Hurley, A. G., and Moore, W. C.: Ann. Surg. **112**:392, 1940.

SUMMARY

Recurrent hemolytic anemia was observed in a 4½ month old boy. Demonstration of hemolytic activity of the patient's serum was accomplished during an acute hemolytic crisis. After splenectomy the hemolytic activity was no longer demonstrable in the patient's serum, and the patient was cured of this disease.

9. Bergenhem, B., and Fåhræus, R.: Ztschr. f. d. ges. exper. Med. **97**:555, 1936.

10. Singer, K.: J. Clin. Investigation **20**:153, 1941.

11. Dameshek, W., and Schwartz, S. O.: New England J. Med. **218**:75, 1938. Farrar, G. E., Jr.; Burnett, W. E., and Steigman, A. H.: Am. J. M. Sc. **200**:164, 1940.

FAMILIAL CHARACTER OF FIBROCYSTIC DISEASE OF THE PANCREAS

PHILIP J. HOWARD, M.D.

DETROIT

Additional information regarding the familial character of fibrocystic disease is afforded by a family in which this condition was proved to occur in 2 children and probably occurred in 3.

Many instances are on record of the deaths of 2 siblings as a result of this condition. A brief review of 120 cases of fibrocystic disease which have been reported has revealed 12 families in each of which 2 children were affected. Andersen¹ stated, "The disease is proved to have occurred more than once in 3 of 23 families and may have occurred in 5 more." Two of the 3 instances Andersen referred to involved siblings who were not twins and 1 involved twins; the last case was cited from Blackfan and Wolbach.² The twins, who died of the disease, were of the same sex, but it is not known whether they were identical. Blackfan and May described another set of twins who died of this disease in the first few days of life, the diagnosis being confirmed at autopsy.³ These twins are not known to have been identical either. There are also a case of 2 siblings reported by Bartlett⁴ and another reported by Kramer,⁵ with proof of the disease by autopsy. In the case of 2 siblings described by Flax⁶ 1 was proved by autopsy to have had the disease; it is probable on clinical grounds that the other had it also. The cases of proved and of probable familial occurrence, with the case reported in the present paper, are summarized in the following tabulation:

Author	2 Proved Cases in Family	2 Probable Cases in Family
Andersen ¹	2	5
Blackfan and Wolbach ²	1	
Blackfan and May ³	1	
Bartlett ⁴	1	
Kramer ⁵	1	
Flax ⁶		1
Howard	1*	

* In addition to the 2 proved cases there was 1 probable case of fibrocystic disease. See text.

1. Andersen, D. H.: Cystic Fibrosis of the Pancreas and Its Relation to Celiac Disease: Clinical and Pathologic Study, *Am. J. Dis. Child.* **56**:344-399 (Aug.) 1938.

2. Blackfan, K. D., and Wolbach, S. B.: Vitamin A Deficiency in Infants, *J. Pediat.* **3**:679 (Nov.) 1933; cited by Andersen.¹

3. Blackfan, K. D., and May, C. D.: Inspissation of Secretion, Dilatation of Ducts and Acini, Atrophy and Fibrosis of Pancreas in Infants: Clinical Note, *J. Pediat.* **13**:627-634 (Nov.) 1938.

4. Bartlett, F. H., in discussion on Andersen.¹

5. Kramer, B., in discussion on Andersen.¹

6. Flax, L. J.; Barnes, M., and Reichert, J. L.: Vitamin A Absorption and Its Relation to Intestinal Motility in Fibrocystic Disease of Pancreas, *J. Pediat.* **21**:475-484 (Oct.) 1942.

Thomas and Schultz⁷ reported 1 case of fibrocystic disease in which the patient had 3 normal siblings, and Jeffrey⁸ reported a similar case in which there were 7 normal siblings. These cases emphasize the factors of chance and scatter, and show that although the factor of disease is in a family, it may not appear more than once.

Recent investigative work of Warkany⁹ has suggested that certain congenital anomalies may be due to dietary deficiency in the maternal diet during gestation. Four sets of twins have been described in the articles on fibrocystic disease. Of the 2 sets of twins from Blackfan and Wolbach² and from Blackfan and May³ respectively all 4 babies died, and all 4 had the disease. Of each of the 2 sets reported by Gamble¹⁰ and by Rasor and Stevenson¹¹ respectively 1 twin was normal and 1 twin had the disease. In the last 2 sets the external conditions, such as diet were of course identical, and the twins were fraternal. Here, then, are 2 instances in which the disease must have been inherited.

In the case reported by Flax⁶ the maternal grandmother had had 6 pregnancies, from which only 1 living child survived, the mother of the patient in the case he reports. A similar fact appears in the history of the family here described—the paternal grandmother was one of a large family in which 7 infants died in early infancy. Although the cause of death in the paternal grandmother's family is not known, it seems likely that the deaths were due to a weakness of the same nature as that appearing in the present generation.

The autopsy reported by Flax,⁶ which showed fibrocystic disease in the pancreas at 45 hours of age, seems to indicate that the disease process was present during the greater part of fetal life. No pathologic condition of the lungs was described, the lungs being considered entirely normal. The patient in case 3 of the present

7. Thomas, J., and Schultz, F. W.: Pancreatic Steatorrhea, *Am. J. Dis. Child.* **56**:336-343 (Aug.) 1938.

8. Jeffrey, F. W.: Cystic Fibrosis of Pancreas, *Canad. M. A. J.* **45**:224-229 (Sept.) 1941.

9. Warkany, J.: Congenital Malformations Induced in Rats by Maternal Nutritional Deficiency: IV. Cleft Palate, *Am. J. Dis. Child.* **65**:882-894 (June) 1943.

10. Gamble, R. C.: Keratomalacia and Cystic Fibrosis of Pancreas, *Am. J. Ophth.* **23**:539-544 (May) 1940.

11. Rasor, R., and Stevenson, C.: Cystic Fibrosis of Pancreas: Case History, *Rocky Mountain M. J.* **38**:218-220 (March) 1941.

report, who died on the twenty-seventh day with extreme infection of the lungs, furnishes an example of the rapidity with which the process can progress.

REPORT OF CASES

The 3 patients whose cases are reported here were children of a physician, Dr. F. The mother has had 6 children, of whom 3 have died of fibrocystic disease and 3 are living and well except that 1 son has paroxysmal tachycardia. The paternal grandmother was one of a large family in which 7 children died in infancy. The cause of so many deaths in one family and in one group of siblings is unknown, but when linked with the present series of 3 deaths in a later group of siblings they suggest a defect of the germ plasm in this family. The data on the infants of the F. family will be reviewed in order.

CASE 1.—The first infant was a girl, born normally at term on Oct. 23, 1935. She began to have peculiar stools at 2 months of age and then began vomiting. A persistent cough followed, with nasal irritation and infection; which did not clear. At 6 months of age bronchopneumonia and death occurred. Autopsy of the lungs revealed multiple abscesses of the lungs and many areas of bronchopneumonia and consolidation. No examination of the pancreas was made. The father states that this infant, in appearance and action, presented a clinical picture identical with that seen in the 2 later infants.

The second infant, a boy, was born normally April 15, 1937 and is alive and well except for being subject to paroxysmal tachycardia.

The third infant, a boy, was born normally June 12, 1938 and is normal in every way.

CASE 2.—The fourth infant, a boy, was born normally May 6, 1941. He seemed well, but presented a feeding problem at once, usually taking less than 3 ounces (90 cc.) per feeding. Administration of a cod liver oil concentrate and ultraviolet irradiation were started at 10 days of age. Six to nine mucus-containing stools were passed daily. The baby was nursed until 6 months of age, supplemental foods being added gradually. Undigested cod liver oil appeared in the stools.

When the patient was 2 months of age a cold and cough developed; the cough persisted for three months. Then wheezing started in the early morning; it gradually became worse and was accompanied by dyspnea, raising of sputum and cyanosis on exertion or crying.

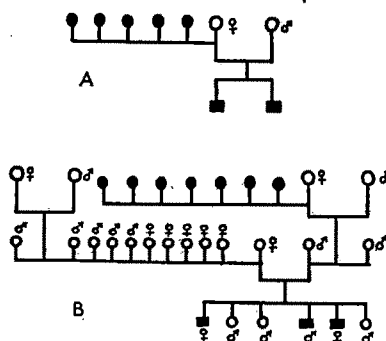
Examination showed stridulous breathing, mucopurulent sputum and coarse rales. The tuberculin test gave negative results. The number of leukocytes increased, and a secondary anemia was present. The stools were bulky, fatty and foul smelling. The level of vitamin A in the blood was 3 U.S.P. units per hundred cubic centimeters (control, 28 U.S.P. units). There was 0.01 mg. per hundred cubic centimeters of carotenoids (control, 0.18 mg.). The sputum showed a heavy growth of staphylococci (coagulase positive) and of type IV pneumococci. Four days after admission 100,000 U.S.P. units of vitamin A was given intramuscularly; the dose was repeated in two days. Fifteen drops of percomorph liver oil was given daily. The milk formula consisted of 5.5 Gm. of pancreatin and 2

ounces (77 Gm.) of banana powder added to 1 quart (0.9 liter) of milk. The level of vitamin A in the blood rose to a low normal value, but no carotenoids were ever demonstrated. Sulfathiazole and blood transfusions were given, but the infant did not survive, death occurring eleven days after his admission to the hospital.

The postmortem diagnosis was: (1) fibrosed and cystic pancreas, with (a) dilatation of the ducts of the pancreas, (b) chronic pancreatitis and (c) malformation congenital hypoplasia of the pancreas; (2) bronchitis; (3) enterogenous cyst of the mesentery, and (4) ascites.

The weight of the pancreas was 10 Gm. The pattern was not that of normal lobules; the surface was finely pitted and trabeculated. Viewed microscopically, the amount of pancreatic parenchymal tissue in each lobule was seen to be decreased. Most of the tissue consisted of islet tissue, dilated ducts and ductules. The lumen was filled with amorphous material. The large ducts toward the head of the pancreas were dilated. The islet tissue was normal.

The major pancreatic duct was patent; consequently the changes could not have been due to obstruction. Marked lobular fibrosis was present, with normal islets, but with atrophic or absent acini. An occasional acinar



Genetic charts showing grouping of infantile deaths. Black disks represent infants dying from unknown causes, black rectangles infants dying from cystic pancreatitis and white disks surviving infants. A, the family reported by Flax. B, family F. of this report.

cell was filled with normal granules of zymogen. The lesion might more accurately be characterized as chronic pancreatitis secondary to or associated with stasis and dilatation than as cystic fibrosis.

CASE 3.—The fifth infant, a girl, was born normally Jan. 12, 1943, weighing 8 pounds and 9 ounces (3,884 Gm.). She was never well. From birth she presented a feeding problem. Breast feeding was discontinued, and protein milk was prescribed because of numerous frothy stools. Coughing started during the first week of life; vomiting was present during the second week. Cyanotic attacks with dyspnea became evident the third week. Roentgenograms of the chest showed consolidation of the upper lobe of the right lung and infiltration throughout the rest of the lung fields. Extreme dyspnea occurred at this time, and vomiting became more marked.

The stool showed 26 per cent fat in the dried residue. The blood diastase was 6.6 units (Myers and Killian) (normal, 15 to 25 units); the blood cholesterol content, 133 mg. per hundred cubic centimeters. Supportive treatment with sulfadiazine, fluids administered parenterally, transfusions and oxygen were given, but unsuccessfully. The infant died Feb. 8, at the age of 27 days; she weighed 7 pounds 2 ounces (3,232 Gm.).

Autopsy revealed fibrocystic pancreatitis, the pancreas weighing 4 Gm. and grossly showing normal lobular markings. On section many dilated ducts filled with acidophilic casts were found throughout all sections taken. The majority of these averaged only 50 to 200 microns in diameter. They were lined by low columnar or cuboidal cells. In addition to these dilated ducts, there were many smaller moderately dilated acini, all filled with acidophilic material. There was diffuse increase in the amount of stroma; frequent conglomerates of lymphocytes were found, but there was no diffuse lymphocytic infiltration. The islet tissue showed no abnormalities. It was average in amount and distribution.

The sixth infant, a boy, was born normally and at the time of writing seems well in every way.

The accompanying genetic charts show the grouping of several early infantile deaths in a single generation of each of 2 families in which fibrocystic disease had appeared. The appearance of the disease in 3 of 6 children of 1 family suggests that the inherited factor is heterozygous, that is, derived from 1 parent only. On the maternal side among 25 cousins, the disease did not appear once; this fact suggests that the inherited factor came from the paternal side only.

SUMMARY

This review shows that there are at least recorded instances of the familial occurrence fibrocystic pancreatic disease.

The literature on the subject describes sets of twins both of whom had the condition and of sets in which only 1 twin was affected.

Extremely unusual grouping of infant deaths occurred in 2 families in which proved fibrocystic disease existed. Two proved and 1 probable instance of the disease in 1 of these families recorded, with a review of deaths of infants in course of three generations. It is suggested that this family furnishes an instance of heterozygous inheritance.

The case reported here adds 1 case of familial fibrocystic disease to the 12 previously recorded.

The details of case 1 were supplied by Dr. W. Cheney, Salt Lake City.

The details of case 2 were supplied by Dr. L. Dickey and Dr. W. B. Friedman, Stanford University School of Medicine. This material has been published in abstract form¹² and has been submitted for publication in detail.

Henry Ford Hospital.

12. Dickey, L. B.: Pulmonary Aspects of Cystic Fibrosis of Pancreas, *California & West. Med.* 57: 42 (July) 1942.

ECTODERMAL DYSPLASIA WITH PARTIAL ANODONTIA

M. MICHAEL COHEN, D.M.D., AND RICHARD WAGNER, M.D.

BOSTON

Ectodermal dysplasia is a rare condition characterized by complete or partial anodontia and by defects in other ectodermal structures. Thoma,¹ in his textbook "Oral Pathology," has given a collective review of 18 cases reported in the literature from 1883 to 1941, and Brodie and Sarnat² contributed another case in 1942.

REPORT OF A CASE

History.—V. M., a girl born April 7, 1941, came under observation at the children's endocrine clinic on Jan. 28, 1944 at the age of 2 years and 8 months, having been referred from the children's clinic of the Boston

Physical Examination.—The patient was a well nourished and well developed girl weighing 25 pounds 12 ounces (11.64 Kg.). She was 36½ inches (92.7 cm.) tall. The skin appeared normal. The lower eyelids were inverted. The bridge of the nose was broadened. There were epicanthal folds (fig. 1). The finger and toe nails were convex and poorly developed; figure 2 shows marked shallow depressions. The toe nails resembled those seen in other trophic disturbances of the ectodermal layer. The hair was smooth and soft, showing no form of alopecia; no lanugo hair was present.

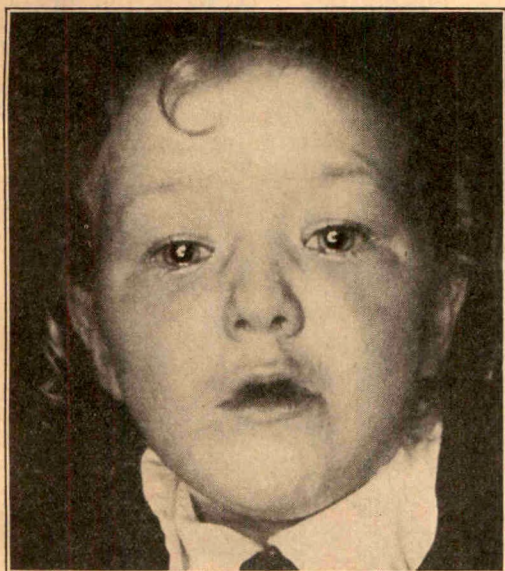


Fig. 1.—V. M. at the age of 2 years 8 months.

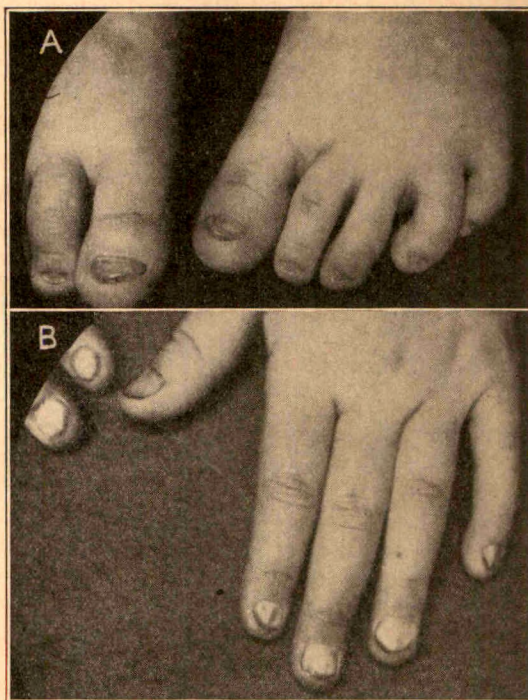


Fig. 2.—A, toe nails of V. M. B, finger nails of V. M.

Dispensary because of the peculiar behavior of her teeth and nails. The mother stated that neither finger nails nor toe nails ever grew; hence they were never cut. The patient neither complained of excessive heat nor suffered from spells of fever or syncope on exposure to the summer sun. She had never been sick and had developed uneventfully. There was no history of familial or hereditary incidence of a similar condition.

From the Department of Pediatrics of Tufts College Medical School, the Children's Department of the Boston Dispensary and the Department of Orthodontia of Tufts Dental School.

1. Thoma, K. H.: Oral Pathology, St. Louis, C. V. Mosby, 1941, pp. 142-148.

2. Brodie, A. G., and Sarnat, B. G.: Ectodermal Dysplasia (Anhidrotic Type) with Complete Anodontia, Am. J. Dis. Child. 64:1046-1054 (Dec.) 1942.

Oral examination of the maxilla revealed two upper caniniform teeth in the canine region and two partially erupted molars. The mandible had two peg-shaped incisors and two atypical canines (fig. 3). The clinical diagnosis of ectodermal dysplasia was made.

Intraoral roentgen examination (fig. 4) revealed no other tooth bud in the maxilla, but the mandible showed another incisor and two molars unerupted without other tooth buds. Altogether there were only eleven teeth detectable by roentgen examination in both jaws.

A lateral roentgenogram of the skull appeared normal and compared favorably with those of other children of this age group.

The carpal development was consistent with the chronologic age.

A psychometric test placed the intelligence quotient of the child at 100.

Biopsy of Skin from Groin (Dr. MacMahon).—Gross examination: The specimen consisted of a minute wedge-shaped scrap of skin.

Microscopic examination: The skin showed an unexplained fresh hemorrhage into the corium. There was no evidence of inflammation or of tumor.

Addenda: The epidermis, the hairs and the sweat glands were free of pathologic conditions. There was no melanosis. There were no sebaceous glands in the section.

The presence of sweat glands is consistent with the statement of the mother that the child did not complain of any inequality of temperature, a circumstance which might be attributed to lack of sweat glands.

COMMENT

This case does not reveal all the signs and symptoms which belong to the classic syndrome

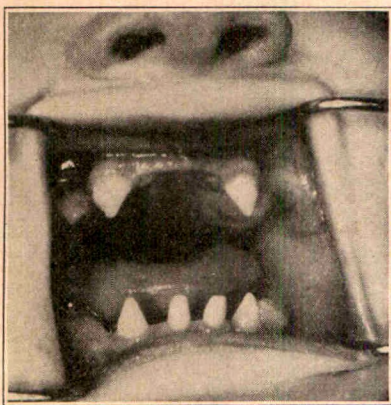


Fig. 3.—Peg-shaped teeth in ectodermal dysplasia.

of ectodermal dysplasia. The skin, hair, iris, sweat and sebaceous glands and finger and toe nails start to develop soon after the second month of fetal life. According to Schour and Massler,³ the first sign of the development of teeth in human beings is seen during the sixth week of embryonic life. If the faulty development is severe and presents itself before the sixth week of fetal life, the teeth will be affected. After the second month of embryonic life the other ectodermal structures may be affected. Various syndromes, however, may result from the involvement of different structures. Theories regarding ectodermal dysplasia seem to indicate that it is sex linked and recessive, being transmitted by female carriers and occurring in males. In certain instances the defect is present in the

3. Cited by Orban, B.: *Oral Histology and Embryology*, St. Louis, C. V. Mosby Company, 1944, pp. 33-52.

female carrier. Other investigators⁴ classify the anomaly as a mendelian dominant character. Of the 20 patients described in the literature, including the patient under discussion (14 males and 6 females), only 10 had pathologic conditions of the skin, which shows that the integument is not always involved. Similarly, in at least half of the reported cases the nails were normal.

Involvement of the teeth with either partial or complete anodontia was manifested in all 20 cases. Peg-shaped incisors were found in 4 of

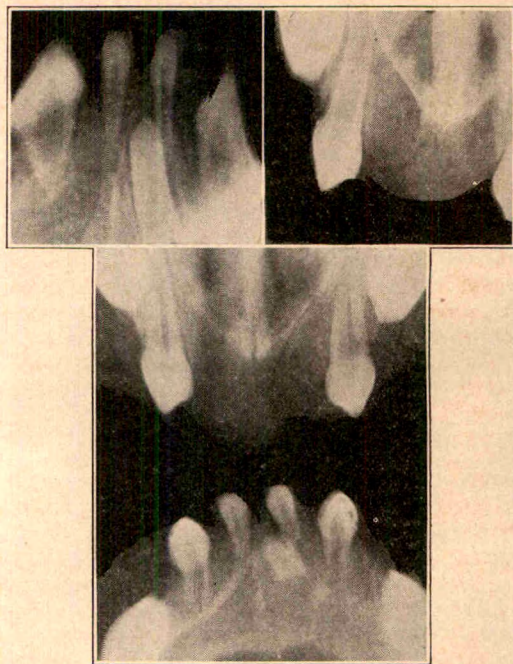


Fig. 4.—Intraoral roentgenogram in ectodermal dysplasia.

12 cases of partial anodontia. Peg-shaped teeth are known in other congenital anomalies. They are seen in mongolian idiocy, in which the brain (ectodermal in origin) is always involved. No severe mental retardation has been reported in any case of ectodermal dysplasia. All the patients were normal except 1, who was reported to be slightly retarded.⁵

520 Beacon Street.

370 Commonwealth Avenue.

4. Holt, L. E., and McIntosh, R.: *Holt's Diseases of Infancy and Childhood*, ed. 11, New York, D. Appleton-Century Company, Inc., 1940, p. 352.

5. Nager, F. R.: Ueber das Vorkommen von Ozäna bei angeborenen Haut- und Zahnanomalien, *Arch. f. Laryng. u. Rhin.* **33**:426, 1920.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

THE ANTIBACTERIAL PROPERTIES OF CRUDE PENICILLIN. A. MURRAY FISHER, *Bull. Johns Hopkins Hosp.* **73**: 343 (Nov.) 1943.

A method is described for the production of crude penicillin. While the potency of the product is less than one-thousandth that of the extract, clinical experience with it is encouraging enough to make the author believe that it will have a place in local therapy for certain infections.

LYTLE, New York.

THE FATE OF THE VIRUS OF LYMPHOGNANULOMA VENEREUM IN INFECTED MICE RECEIVING SULFONAMIDE THERAPY. ENID C. RODANICHE, *J. Infect. Dis.* **73**:173 (Nov.-Dec.) 1943.

There is active multiplication of the virus of lymphogranuloma venereum in the brains of mice treated with sulfadiazine and sulfathiazole.

The virus is not recovered from the spleens of such animals in the great majority of instances, although it is readily isolated from the spleens of untreated animals.

Paraaminobenzoic acid exerts some antagonism to the action of sulfathiazole on this virus.

The virus of lymphogranuloma does not become resistant to sulfonamide compounds within seven mouse passages.

TOOMEY, Cleveland.

SURVIVAL OF BACTERIA ON THE SILVER COMMUNION CUP. WILLIAM BURROWS and ELIZABETH S. HEMMENS, *J. Infect. Dis.* **73**:180 (Nov.-Dec.) 1943.

Evidence is presented which indicates that bacteria swabbed on the polished surface of a silver chalice die off rapidly. Experiments on the transmission of test organisms from one person to another by common use of a chalice showed that only approximately 0.001 per cent of the organisms are transferred even under the most favorable conditions; when conditions approximated those of actual use, no transmission could be detected. Only small numbers of bacteria from the normal mouth could be recovered from the chalice immediately after its use by 4 persons. It is concluded that in practice the silver communion cup is not an important vector of infectious disease.

TOOMEY, Cleveland.

THE TREATMENT OF MENINGOCOCCIC MENINGITIS. ANNETTE C. WASHBURN, *Wisconsin M. J.* **42**:1239 (Dec.) 1943.

Meningococcic meningitis requires immediate and intensive action. The following procedures are listed: prompt spinal tap (or cisternal if necessary) if there are definite or suspicious signs of meningitis; cell count and differential count; determinations of sugar and protein and a colloidal gold test; Wassermann test, and stain for predominating organism and culture. Of these, the cell count, the test for sugar and the identification of predominating organisms should be done immediately. Since a cloudy fluid may also be found in syphilitic meningitis, brain abscess, sinus thrombosis, extradural abscess and occasionally poliomyelitis, these conditions

should be differentiated. A blood culture should also be done at this time.

In treatment, large initial doses of sulfadiazine and early intensive medication are essential. Administration of sulfadiazine should not be completely discontinued for ten or twelve days. It is best given by mouth, or by nasal catheter if the patient is comatose. The sodium salt (5 per cent solution) may be given by intravenous drip; care should be taken to avoid leakage into tissue and not to give a blood transfusion or an intravenous injection of dextrose solution at the same time.

A solution of sodium sulfadiazine, 5 Gm. in 500 cc. of isotonic solution of sodium chloride (1 per cent), may be given subcutaneously at the rate of 250 to 300 cc. per hour. Sulfadiazine should not be given intrathecally, intramuscularly or by rectum. When possible, except in critical conditions, the sulfonamide drug is best given orally. Sodium bicarbonate in 1 to 2 Gm. doses reduces the formation of crystals. Daily clinical examination for mental status (alertness, confusion, etc.), meningeal changes, otitis or deafness, involvement of the chest and heart, full bladder, orchitis, petechiae, edema, state of reflexes, type of breathing and intake and output should be made. A blood count, urinalysis and determination of the blood level of sulfadiazine (desirable concentration, 15 to 18 mg.) should be done the first week. For an adult the fluid intake should not be under 3,500 cc. or the output below 1,500 cc. per twenty-four hours.

In addition to the initial spinal tap, one or two more may be done after the eighth or ninth day to determine the degree of cure or to relieve increased pressure. Sedation, including administration of codeine, may be wise. If the therapy is not promptly effective a change in the type of sulfonamide compound (to sulfamerazine, etc.) or the use of antimeningococcus serum is indicated.

JANNEY, Wauwatosa, Wis.

Metabolism; Infant Feeding; Milk and Other Foods

STUDIES OF CALCIUM AND PHOSPHORUS METABOLISM IN THE CHICK. EVAN W. MCCHESENEY, *J. Nutrition* **26**:487 (Nov.) 1943.

Evan W. McCchesney has determined the relative effectiveness of vitamins D₂ and D₃ and dihydrotachysterol when administered parenterally to the chick in propylene glycol and corn oil. Dihydrotachysterol was 300 per cent more effective than vitamin D₃ orally; however, parenterally it was on the average only about 20 per cent more effective. D₃ was somewhat better absorbed from the digestive tract than D₂.

FREDEEN, Kansas City, Mo.

THE NUTRITIVE VALUE OF PROTEIN. ROBERT A. STEWART, GEORGE W. HENSLEY and F. N. PETERS JR., *J. Nutrition* **26**:519 (Nov.) 1943.

Robert A. Stewart and others conclude that normal cooking does not impair the quality of protein; however, severe heat treatment by means of the explosion technic destroyed the quality of oat protein considerably.

FREDEEN, Kansas City, Mo.

Vitamins; Avitaminoses

RIBOFLAVIN AND THIAMINE INTERRELATIONSHIPS IN RATS AND IN MAN. JOSEPH W. FERREBEE and NORMAN WEISSMAN, *J. Nutrition* **26**:459 (Nov.) 1943.

J. W. Ferree and N. Weissman report that their observations failed to demonstrate that thiamine deficiency in itself has an effect on riboflavin metabolism. The increased excretion of riboflavin appears to be an unspecific phenomenon of the late stages of thiamine deficiency related to the rapid metabolism of tissues that occurs when the thiamine requirements can be satisfied only by loss of tissue.

FREDEEN, Kansas City, Mo.

LOSSES OF B VITAMINS DUE TO COOKING OF FOODS. VERNON H. CHELDELIN, ALETHEA M. WOODS and ROGER J. WILLIAMS, *J. Nutrition* **26**:477 (Nov.) 1943.

The authors present determinations of cooking losses in 30 foods of riboflavin, nicotinic acid, pantothenic acid, biotin, inositol and folic acid.

FREDEEN, Kansas City, Mo.

A STUDY OF NORMAL HUMAN REQUIREMENTS FOR ASCORBIC ACID AND CERTAIN OF ITS METABOLIC RELATIONSHIPS. HELEN J. PURINTON and CECILIA SCHUCK, *J. Nutrition* **26**:509 (Nov.) 1943.

The daily human requirements for ascorbic acid were found to be in excess of 100 mg. per day for the young adult; and for adults between 25 and 50 years of age, less than 100 mg. Purinton and Schuck note that the requirements for ascorbic acid are influenced by certain factors, such as the basal metabolic rate and the hemoglobin level and the metabolism of citric acid.

FREDEEN, Kansas City, Mo.

DETERMINATION AND CONTENT OF CAROTENE AND VITAMIN A IN WISCONSIN BUTTER. SOLL BERL and W. H. PETERSON, *J. Nutrition* **26**:527 (Nov.) 1943.

Soll Berl and W. H. Peterson note that 75 per cent of the total natural butter pigment in summer was carotene; in winter 60 to 65 per cent was carotene. The summer butter (July and September) averaged about 18,000 U. S. P. units of vitamin A per pound; winter butter (January), 10,500 U. S. P. units per pound, and spring butter (March), 9,500 U. S. P. units per pound. Storage of butter as long as eight months did not result in a loss of carotene or vitamin A.

FREDEEN, Kansas City, Mo.

THE ASCORBIC ACID REQUIREMENTS OF SCHOOL-AGE GIRLS. VIVIAN M. ROBERTS, MARGARET HESSLER BROOKES, LYDIA J. ROBERTS, PEGGY KOCH and PEGGY SHELBY, *J. Nutrition* **26**:539 (Nov.) 1943.

The ascorbic acid requirement of preadolescent girls of 6 to 12 years for adequate saturation with vitamin C was 62 to 72 mg. daily.

FREDEEN, Kansas City, Mo.

THE RETENTION OF VITAMINS IN VEAL AND LAMB DURING COOKING. J. M. MCINTIRE, B. S. SCHWEIGERT and C. A. ELVEHJEM, *J. Nutrition* **26**:621 (Dec.) 1943.

J. M. McIntire and others found that almost the entire decrease in the weight of meat during cooking

was due to loss of water. Roasted and broiled meats retained more moisture than those braised and stewed; and vitamin retention corresponded with water retention in every case.

FREDEEN, Kansas City, Mo.

INFLUENCE OF INCREASING DOSES OF THIAMINE AND RIBOFLAVIN ON EFFICIENCY OF THEIR UTILIZATION. BARNETT SURE and ZENAS W. FORD JR., *J. Nutrition* **26**:659 (Dec.) 1943.

B. Sure and Z. W. Ford Jr. conclude that the animal organism has only a very limited capacity for storing these two components of the vitamin B complex. A quantitative metabolism study was made of the influence of increasing doses of thiamine and riboflavin on their efficiency of utilization. On higher levels of intake the efficiency of utilization decreased; this suggests that part of the losses of thiamine and riboflavin in metabolism were caused by their destruction in the tissues.

FREDEEN, Kansas City, Mo.

Hygiene; Growth and Nutrition; Public Health

WHAT'S WRONG WITH OUR SCHOOL HEALTH SERVICE? HAROLD MITCHELL, *New York State J. Med.* **43**:527 (March 15) 1943.

This paper is one in a panel discussion of school health services. We need medical leadership rather than lay control to determine the quality of medical service to be given in the schools. Physicians have been required to examine too many children, and the examinations have been too superficial. In order to improve these services it is suggested that a medical society advisory committee should be recognized as a part of every school system.

"I have heard state education officials stress the health educational value of the health examination, but I have never discovered that they appreciate what bad education it is for parents and children to get a false sense of security from inadequate examinations in school." The physician in the school should act as an adviser, consultant and educator, not as a mere examiner.

AIKMAN, Rochester, N. Y.

WAYS TO MORE EFFECTIVE SCHOOL HEALTH SERVICE. GEORGE WHEATLEY, *New York State J. Med.* **43**:529 (March 15) 1943.

This paper is one in a panel discussion of school health services. Medical records should be modernized and then carefully preserved. It is worth while to train volunteer aids to do this work. Teachers may make semiannual tests of vision and measure the height and weight of the child. Audiometer tests may be made by technicians. By the use of lay assistants, the physician will be enabled to give his time to more important matters. Increased participation of the private physician is also advised.

AIKMAN, Rochester, N. Y.

Prematurity and Congenital Deformities

COMBINED ANTERIOR AND POSTERIOR SPINA BIFIDA IN A LIVING NEONATAL HUMAN FEMALE. R. L. DE C. H. SANDERS, *Anat. Rec.* **87**:255 (Nov.) 1943.

It was observed that in a 2 day old baby with a mucosal mass projecting over the lumbosacral region feces were passed through this and per anum. Death at 5 months was followed by postmortem examination, which revealed a fistula connecting the colon through the cleft in the vertebrae; the cord was divided into

two portions below, having two sets of nerves from the left side and one from the right. Thirty-seven cases of this condition have been reported.

SNELLING, TORONTO, CANADA.

THE EFFECT ON THE FETUS OF PENTOBARBITAL SODIUM AND PENTOTHAL SODIUM. ROBERT DREISBACH and FRANKLIN F. SNYDER, J. Pharmacol. & Exper. Therap. **79**:250 ((Nov.) 1943.

An investigation of the effects of pentobarbital sodium and pentothal sodium on the fetus was made because these drugs are said to be used extensively in obstetric practice. The fetuses (rabbit) were observed through the uterine wall, which had been exposed by laparotomy after section of the lumbar portion of the spinal cord with the area under procaine anesthesia. Pentcthal sodium was found to be relatively nontoxic to the fetus, for as much as 55 mg. per kilogram of maternal body weight by vein to the mother rabbit had relatively little cumulative effect on the fetus.

Fetal apnea following the injection of pentcthal sodium into the maternal animal was caused by the drug and was not due to anoxemia, since analyses of fetal blood showed that the content of oxygen and of carbon dioxide remained normal.

PILCHER, Cleveland.

Newborn

NUTRITION STUDIES DURING PREGNANCY: IV. RELATION OF PROTEIN CONTENT OF MOTHER'S DIET DURING PREGNANCY TO BIRTH LENGTH, BIRTH WEIGHT AND CONDITION OF INFANT AT BIRTH. B. S. BURKE, V. V. HARDING and H. C. STUART, J. Pediat. **23**:506 (Nov.) 1943.

This paper is one of a series dealing with the importance to both mother and infant of adequate nutrition during pregnancy. The material presented was collected as a part of the research program undertaken by the department of child hygiene of the Harvard School of Public Health at its Center for Research in Child Health and Development. The mothers and infants considered are the same as described in the introductory article of the series (Burke, B. S.; Beal, V. A.; Kirkwood, S. G., and Stuart, H. D.: Nutrition Studies During Pregnancy, *Am. J. Obst. & Gynec.* **46**:38-52 [July] 1943) in which the group studied and the methods employed are described in detail.

The average daily content of protein in the diet of each woman during the latter part of pregnancy has been estimated in grams. In this group of 216 women only 10 per cent consumed diets which contained the amount of protein (85 Gm.) recommended by the Food and Nutrition Board of the National Research Council for that period (fourth through the ninth month), 22 per cent consumed between 70 and 84 Gm., 68 per cent consumed less than 70 Gm. of protein daily and 38 per cent less than 55 Gm. daily, or diets which were considered poor or extremely poor in this important nutritional essential during a period of rapid growth and development of the fetus.

A significant relationship ($+0.80 \pm 0.03$) was found to exist between the protein content of the antepartum diet of the mother and the length at birth of the infant. With allowance made for the height of the mother, the partial correlation between the length of the baby and the amount of total protein in the diet of the mother in the latter part of pregnancy is about the same ($+0.78 \pm 0.03$). If separate calculations are made for boys and girls this increase in birth length is demonstrated with

each additional increment (10 Gm.) of protein in the antepartum diet. An increase in weight at birth was also demonstrated with each additional increment (10 Gm.) of protein in the diet of the mother during pregnancy. This relationship, while significant, is not as striking as the correlation between the amount of protein in the maternal diet during pregnancy and the length of the infant at birth. The infant boys were found to be somewhat longer and heavier than the infant girls for any given amount of protein in the diet of the mother. When the protein content of the diet of the mother was under 45 Gm. daily the average length at birth of the infant boys was 47.6 cm. and of the infant girls 46.8 cm.; their average weights at birth were 6 pounds 8 ounces (2,950 Gm.) and 5 pounds 14 ounces (2,650 Gm.) respectively. In contrast when the protein content of the mother's diet was 85 Gm. or more daily the average length at birth of the boys was 53.3 cm. and of the girls 52.4 cm.; their average weights at birth were 9 pounds 2 ounces (4,150 Gm.) and 8 pounds 8 ounces (3,850 Gm.) respectively.

A significant relationship is also shown between the physical ratings assigned by the pediatrician to the infants at birth and within the first two weeks of life and their weights and lengths at birth. The amount of protein in the diet of the mother during pregnancy appears to be an extremely important factor in determining the general physical condition of the infant at birth.

It would appear from this study that from the standpoint of length, weight and general physical well-being of the infant at birth the diet of the mother should be liberally supplied with protein during pregnancy. In terms of simple everyday foods it is clear that if protein is not the key factor other factors which may be important are adequately provided if the antepartum diet is high in protein rich foods. The foods chiefly responsible for the protein in the diets of these women were meat, poultry, eggs, milk, cheese and fish; the nonanimal sources were largely cereal grains.

For practical purposes this study indicates that a diet containing less than 75 Gm. of protein daily during the latter part of pregnancy tends to make the infant short, light in weight and likely to receive a low pediatric rating in other respects.

BURKE, Boston.

LIVER FUNCTION IN THE NEWBORN INFANT. GEORGE W. SALMON and ELLEN EHRENFEST RICHMAN, J. Pediat. **23**:522 (Nov.) 1943.

In a series of studies of newborn infants, determinations of the packed cell volume and of the icterus indexes revealed no relationship between the degree of destruction of blood cells and the severity of the icterus.

Visible icterus might not be present in a newborn infant even though the icterus index was considerably above 15, the threshold level commonly accepted for adults. If the icterus index remained elevated, however, visible icterus appeared. The appearance of visible icterus is a function not only of the degree of hyperbilirubinemia but of the length of time the condition has persisted.

There was no difference in the ability of the liver to excrete sulfobromophthalein in the newborn infants whose icterus index rose to 20 or above and in those whose icterus index remained below 20. Moreover, the ability of the livers of newborn infants to excrete this dye was similar to that reported for adults.

The reaction to the cephalin-cholesterol flocculation test of Hanger showed varying degrees of positivity during the first few days of life and tended to become negative toward the end of the first week of life. There was no obvious difference in the results obtained for the

newborn infants whose icterus index rose to 20 or above and for those whose icterus index remained below 20. It will be difficult to interpret these results until the fundamental reaction of the cephalincholesterol flocculation test is adequately explained.

SALMON, St. Louis.

UNUSUAL INFECTIONS IN THE NEWBORN CAUSED BY STAPHYLOCOCCUS AUREUS. RUTH G. ALEMAN, New Orleans M. & S. J. **96**:207 (Nov.) 1943.

Three instances of recovery from Staphylococcus aureus infections are reported. All 3 patients received sulfonamide drugs, plus other appropriate treatment. One patient with septicemia did not survive.

BERKLEY, Beverly Hills, Calif.

ERYTHROBLASTOSIS FOETALIS AND ITS RELATIONSHIP TO TRANSFUSION. REACTIONS AND ACCIDENTS. THOMAS A. LEONARD, Wisconsin M. J. **42**:1032 (Oct.) 1943.

In 1932 Blackfan, Diamond and Baty concluded regarding the erythroblastotic baby that:

1. There is universal edema, from severe to minimal.
2. Jaundice, "mahogany-brown" typically, is present at birth or appears in forty-eight hours.
3. Early anemia, often obscured by jaundice at first, is always noticeable by the fifth day.
4. Edema, jaundice and anemia may be present in any combination or degree.
5. The infant shows marked lassitude, exhaustion or semishock. It is difficult to feed and gains weight slowly.
6. The heart is uniformly enlarged.
7. The infant shows hemorrhagic tendencies; if not visible during life, these tendencies are always evident at autopsy.
8. Pathologically, there are always extramedullary centers of erythroblastosis and some enlargement of the liver and spleen. Other pertinent facts developed since are:

1. The frequency of erythroblastosis is about 8 in every 1,000 births.
2. Erythroblastosis is responsible for about 5 per cent of all fetal mortality.
3. There is a familial occurrence. In 50 to 80 per cent of instances, after one occurrence subsequent offspring will be affected.
4. Race has no influence.
5. About one third of the mothers of erythroblastotic babies have symptoms of toxemia.
6. The mothers show poor gain in weight, high incidence of hydramnios, decreased fetal activity and usually premature labor.
7. There may be amber-colored liquor amnii or golden vernix.
8. The placenta is always large, heavy and edematous; this condition is often detected by roentgenography.

Theories of cause have been:

1. A primary metabolic disturbance or a dominant mutation of the germ cell of either parent.
2. Failure to inherit an antihemolytic substance.
3. Passive sensitization of the fetus against its own red blood cells by agglutinins from the maternal circulation.
4. Fetal hepatic dysfunction.

In 1938 Darrow suggested that erythroblastosis fetalis might be due to an antigen-antibody reaction between the infant's and the mother's blood.

In 1940 Landsteiner found that 85 per cent of all persons had red blood cell agglutinogens which reacted to rhesus monkey-immunized rabbit serum (Rh-positive blood) and that 15 per cent did not (Rh-negative blood).

In 1940 Wiener and Peters applied the principle of the Rh factor to transfusion reactions.

Levine in 1941 showed that 91 per cent of the mothers of infants affected with erythroblastosis had Rh-negative blood, as compared with 15 per cent in the general population, and that 100 per cent of the fathers had Rh-positive blood. The ordinary grouping and cross matching of the bloods of the donor and the recipient do not reveal these subgroup factors.

Erythroblastosis fetalis is definitely caused by the hereditary transmission of the Rh-positive factor from the father to the fetus and the resultant antibody-antigen reaction between the mother and the fetus.

Acute Contagious Diseases

QUANTITATION OF MUSCULAR FUNCTION IN CASES OF POLIOMYELITIS AND OTHER MOTOR NERVE LESIONS. ROBERT S. SCHWAB, ARTHUR L. WATKINS and MARY A. B. BRAZIER, Arch. Neurol. & Psychiat. **50**:538 (Nov.) 1943.

The authors describe the technic of measurement of electrical excitability by voltage-capacity curves. They think that it is essential to have an accurate objective test of muscular function in cases of lesions of motor nerves and they suggest that this is the best method for determining this function.

BEVERLY, Chicago.

CONCURRENT MENINGOCOCCAL MENINGITIS AND SALMONELLA BACTEREMIA. ERWIN R. NETER, J. Pediat. **23**:562 (Nov.) 1943.

A case of concurrent meningococcal meningitis and bacteremia due to Salmonella cholerae suis is presented. A culture of blood taken on the day after the patient's admission to the hospital revealed S. cholerae suis. The patient was given 0.5 Gm. of sulfathiazole by mouth every four hours for seven days. On the fourth day after admission the temperature returned to normal and remained so until the patient was discharged, cured of both meningococcal meningitis and salmonella bacteremia. S. cholerae suis was present in the blood of the patient over a period of five days. Specific agglutinations in high titer against the paratyphoid bacillus developed in the course of the illness. The relationship between the two infections is discussed.

SCOTT, Louisville, Ky.

NEW DEVELOPMENTS IN INFANTILE PARALYSIS. DON W. GUDAKUNST, New York State J. Med. **43**:1514 (Aug. 15) 1943.

Gudakunst reviews the new observations on poliomyelitis up to May 1943. The National Foundation for Infantile Paralysis, Inc., has carefully studied the work of Sister Kenny. After reports that her methods relieved pain, reduced stiffness and prevented contractures, the Foundation "recommended that the method of treatment and the concept on which it was based be made available to the medical and public health authorities of this country for their use, if so desired. No other

claims were made by the National Foundation with respect to this treatment."

AIKMAN, Rochester, N. Y.

STUDIES ON THE TREATMENT OF EPIDEMIC EXPERIMENTAL POLIOMYELITIS WITH POLIOMYELITIS ANTISTREPTOCOCCIC SERUM: SUMMARY OF RESULTS. E. C. ROSENOW, Proc. Staff Meet., Mayo Clin. **18**:403 (Oct. 20) 1943.

Rosenow summarizes the results of his studies, which, he believes, indicate a causal relation of streptococci to poliomyelitis, the proof being the production of the classic clinical and pathologic picture of poliomyelitis in monkeys with virus derived from streptococci.

In 1916 Rosenow first immunized horses with freshly isolated strains of living streptococci of poliomyelitis, which he asserts that he obtained from human beings. Later he employed strains freshly isolated from the spinal cords of monkeys which had died of experimental poliomyelitis after inoculation with the virus. At the end of the period of immunization the antistreptococcus horse serum, in extremely high dilutions, agglutinated specifically the poliomyelitis type of streptococci. It protected rabbits against inoculation with the streptococci and monkeys against inoculation with poliomyelitis virus.

Immune serum was first employed with patients during the 1917 epidemic. The serum was administered as soon as the diagnosis was established. The mortality rate in an untreated group of 23 patients was 35 per cent. Of the 58 patients who received the serum 10 (17.2 per cent) died; of these, 7 were practically moribund at the time of the first serum treatment. Of 51 patients, therefore, 3 for whom the serum might have been beneficial died. Paralysis did not develop in any of the 19 patients to whom serum treatment was given before this condition had appeared, and all promptly recovered. Patients who showed evidence of bulbar involvement, even those in the early stages of partial or complete coma, often responded favorably to administration of the serum, provided it was given soon after the onset of these symptoms.

The current method of preparation of the antiserum is as follows: Freshly isolated streptococci are placed in dense suspension in glycerin (2 parts) and a 25 per cent solution of sodium chloride (1 part) and kept in a refrigerator. Antigenic specificity is preserved almost indefinitely. All subsequent batches of antistreptococcus serum used for treatment are prepared by diluting such dense suspensions as are needed for injections throughout the period of immunization.

Of the total of 2,664 patients who were treated with the serum, 252 (9.6 per cent) died, as compared with 583 (21.3 per cent) of 2,737 patients in the same epidemic who were not given serum. In experiments with monkeys the animals who were given serum exhibited a mortality rate one-half to one-third that of the untreated control group.

In the course of these studies, the euglobulin fraction of poliomyelitis antistreptococcus serum was found diagnostic when employed in a cutaneous test. Ninety-two per cent of 324 persons ill with poliomyelitis for from one to fifteen days showed an erythematous patch of 5 sq. cm. or more in from five to ten minutes after the intradermal injection of the euglobulin fraction.

Rosenow states that objections to the general adoption of this treatment have been removed since his recent demonstration of microdiplococci in filtrates of the virus. Further, the classic picture of the disease has been produced in monkeys with virus derived from

streptococci, and the diagnostic and preventive action of the serum has been demonstrated.

GUTTMAN, New York.

[ARCH. NEUROL. & PSYCHIAT.]

THE USE OF SULPHONAMIDES IN MEASLES. ROBERT SWYER, Brit. J. Child. Dis. **40**:63 (July-Sept.) 1943.

Eleven hundred and ninety-three cases of measles occurring in the 1940-1941 epidemic were studied. Three hundred and twenty-four patients received either sulfanilamide or sulfapyridine for a short period immediately after admission to the hospital; 869 did not unless complications arose necessitating the use of these drugs for treatment.

The complication rate was reduced from 13.7 per cent to 11.4 per cent, the average length of stay from twelve and two-tenths to ten and eight-tenths days. The case mortality of bronchopneumonia was approximately halved.

The author concludes that a short course of prophylactic treatment is not worth while.

LANGMANN, New York.

AGE FOR DIPHTHERIA IMMUNIZATION IN SOUTH AFRICA. N. L. MURRAY, South African M. J. **17**:334 (Nov. 13) 1943.

Since 1921 the incidence of diphtheria in South Africa has more than trebled. In 1941 there were 3,317 cases reported and 130 deaths. Many of the patients were below the age of 1 year, and 50 per cent were under 5 years. Half the total deaths from diphtheria, of Europeans at any rate, occur by the fourth year of life. One reason for this state of affairs is that the majority of the persons being immunized are of late preschool age or of school age; another reason is that not nearly enough susceptible persons are being immunized. Alum-precipitated toxoid in two doses with an interval of four weeks between doses is recommended for all children. The earlier the inoculation after the age of 6 months the better. For adults a preliminary Schick test with a Moloney test simultaneously is advisable. Immunization of adults can be done in selected instances with Ramon's anatoxin (three injections) or with alum-precipitated toxoid (two injections, as for children).

GONCE, Madison, Wis.

THE SIGNIFICANCE OF C. DIPHTHERIAE GRAVIS IN THE EPIDEMIOLOGY OF DIPHTHERIA. J. F. MURRAY, South African M. J. **17**:337 (Nov. 13) 1943.

Murray summarizes the significant features of the three strains of *Corynebacterium diphtheriae* (mitis, intermedius and gravis) in the epidemiology of diphtheria.

GONCE, Madison, Wis.

Acute Infectious Diseases

THE TREATMENT OF AMOEBIC DYSENTERY. HORACE W. SOPER, Am. J. Digest. Dis. **10**:407 (Nov.) 1943.

The author pleads for the use of the intravenous rather than the subcutaneous or the intramuscular route in the administration of emetine hydrochloride. He states the belief that he accomplishes more by giving $\frac{1}{2}$ grain (0.03 Gm.) intravenously daily for seven days than do others by giving 1 grain (0.06 Gm.) subcutaneously or intramuscularly daily for twelve days.

Following seven consecutive daily intravenous doses of emetine hydrochloride, a seven day course of acetar-

sone is given. This consists of one 0.25 Gm. tablet of acetarsone three times daily, before meals.

MORRISON, Savannah, Ga.

ALLERGIC MANIFESTATIONS IN ATOPIC INDIVIDUALS FOLLOWING INJECTION OF TETANUS TOXOID. HARRY SWARTZ, J. Allergy **14**:544 (Nov.) 1943.

The author reports on 2 adults, a man and a woman, in whom a reaction developed following the injection of fluid tetanus toxoid: In the man an erythematous pruritic papular eruption developed and persisted for two years, until hyposensitization was tried with a beginning dose of 0.1 cc. of 1:10,000 solution of tetanus toxoid.

The patient's skin welted when scratched, and he gave a history of having had dermatitis due to ivy. There was a prominent history of allergy in his family.

The woman had severe pruritus after a second injection of fluid toxoid. The symptoms decreased gradually after several months. There was a history of subclinical allergy in the patient and in her family.

HOYER, Cincinnati.

ANAPHYLAXIS AFTER INJECTION OF TETANUS TOXOID. WALTON M. EDWARDS, J. Allergy **14**:552 (Nov.) 1943.

Edwards reports a case of anaphylactoid reaction following the third injection of fluid toxoid.

The patient had a severe cutaneous reaction to four brands of fluid toxoid and to peptone beef heart extract and veal infusion. A peptic meat digest and veal infusion were ingredients of the toxoid he had received.

HOYER, Cincinnati.

OBSERVATIONS ON TETANUS IMMUNIZATION: THE DOSAGE OF ALUM-PRECIPITATED TOXOID AND THE USE OF FLUID TOXOID AFTER TRAUMA. JOHN J. MILLER JR. and J. B. HUMBER, J. Pediat. **23**:516 (Nov.) 1943.

With the production of tetanus antitoxin as a measure of potency, alum-precipitated tetanus toxoid was found superior to fluid tetanus toxoid. The question arises: Should two or three injections of alum toxoid be given?

A comparison was made of the tetanus antitoxin titers attained in two groups of infants and little children. The first group, 68 children, received two injections of 1.0 cc. each of combined alum-precipitated diphtheria and tetanus toxoid during a minimum interval of eight weeks followed by a third injection of 0.5 cc. of alum-precipitated tetanus toxoid at least sixteen weeks later. The second group, 93 children, received the first two injections but not the third.

Antitoxin titrations were performed on several occasions in each group for a year after completion of the immunization. All children in both groups tested two to four weeks after completion of their injections produced at least 0.1 unit of tetanus antitoxin. At this time only one of 39 children who had received three injections showed less than 1.0 unit of antitoxin. In the other group 20 of 46 exhibited titers under 1.0 unit. Thereafter the median antitoxin level dropped more rapidly in the "two injection" group. Between nine and fifteen months after completion of the injections the principal difference in the two groups was the proportion of children with levels of antitoxin above and below the 0.1 unit level. This difference greatly favored the group of children who had received three injections.

Hall has shown, and others including ourselves have confirmed, that basic immunity is conferred by two injections of alum-precipitated toxoid. Basic immunity, then, is all that is desired providing that tetanus toxoid will be administered at the time of trauma and that all basically immunized persons respond to this "booster" injection rapidly. If, however, the intent of the immunizing procedure is to protect the subject completely against tetanus for a given period, even when reinjection is unintentionally omitted after trauma, the quantity of circulating antitoxin becomes of great importance. Therefore, a course of injections which result in the maintenance of levels above 0.1 unit for a year would seem advisable. Annual reinjection would also be indicated.

Comparative studies on the type and dose of toxoid to be used for "booster" injections at the time of trauma can readily be made. Data concerning the speed of antitoxin production following reinjections of alum-precipitated and of fluid toxoid was available for the groups of children discussed. The basic course of immunization consisted of the two or three injections of alum-precipitated tetanus toxoid. Reinjections were given twelve to fifteen months after the last injection of the basic course. One cubic centimeter of fluid toxoid and 0.5 cc. of alum-precipitated toxoid were the doses used. Blood for antitoxin titrations was obtained at the time of reinjection and usually four, five or seven days later. The range of antitoxin levels at the time of reinjection was comparable in the two groups. The average increase among the children in the group given fluid toxoid four or five days after reinjection was tenfold, whereas among the group receiving alum-precipitated toxoid it was fivefold. Seven days after reinjection the average increase in the group given fluid toxoid was one hundred fold, as compared with fortyfold in the group receiving alum-precipitated toxoid.

MILLER JR., San Francisco.

POTENTIALITIES IN THE SCHOOL FOR RHEUMATIC FEVER CONTROL. GEORGE M. WHEATLEY, New York State J. Med. **43**:1947 (Oct. 15) 1943.

This is part of a symposium on rheumatic fever.

Teachers should be instructed in the detection of illness in children. There should be regular medical supervision of children known to have cardiac disease, and expert cardiac consultation services should be provided.

AIKMAN, Rochester, N. Y.

SULFAPYRIDINE FASTNESS IN A CASE OF PNEUMOCOCCIC MENINGITIS. CLARK S. SHUMAN, New York State J. Med. **43**:2037 (Nov. 1) 1943.

This 3-year old girl with type XVIII pneumococcic meningitis of unknown origin at first responded to and then became resistant to sulfapyridine. Rabbit serum was given, but the child died on the twenty-fifth day. There was no autopsy report.

AIKMAN, Rochester, N. Y.

ACUTE ASCARIASIS IN CHILDREN. P. B. FERNANDO and S. BALASINGHAM, Indian J. Pediat. **10**:149 (Oct.) 1943.

Ascariasis is widespread and is an important factor in juvenile health in Ceylon. It ranked sixth in importance in causes of admission to Lady Ridgeway Hospital for Children in Colombo and third in causes of death. Girls were affected more often than boys. The symptoms may be negligible, or they may simulate acute intestinal infection, acute conditions within the

abdomen, cerebral disease or acute respiratory disease. The symptoms are most apt to be due to absorption of toxic products from dead rather than live worms. Complications may be due to the migratory activities of the worms.

TENNEY, Madison, Wis.

BLACKWATER FEVER. T. E. WILSON, M. J. Australia 2:414 (Nov. 20) 1943.

The author reports 2 cases of blackwater fever in which recovery was seemingly induced by alkalinization of the urine (to inhibit the deposition of acid hematin in the renal tubules), repeated blood transfusion (to prevent anoxic changes in the renal tubules and to maintain the filtration pressure in the kidneys), administration of large amounts of fluid by mouth and intravenously and temporary avoidance of antimalarial drugs.

GONCE, Madison, Wis.

Chronic Infectious Diseases

MAPHARSEN IN THE TREATMENT OF CONGENITAL SYPHILIS. GIRSCH D. ASTRACHAN and VAN ALSTYNE CORNELL, J. A. M. A. 121:746 (March 6) 1943.

Astrachan and Cornell consider mapharsen a good drug for use in treatment of late congenital syphilis and of interstitial keratitis. Dr. John E. Rauschkolb in his discussion of this paper disagrees with the authors as to the usefulness of mapharsen in treatment of interstitial keratitis.

Astrachan and Cornell believe that 0.75 mg. per kilogram of weight should be the maximum dose for patients with any form of congenital syphilis. It is less toxic to children than to adults and can be given intramuscularly to selected patients if all attempts at intravenous therapy have failed.

In 7 of 10 cases of early congenital syphilis the patient's serologic reaction was reversed partly or completely after an average of seventeen and three-tenths injections of mapharsen had been administered.

HENSCHEL, Denver.

[ARCH. DERMAT. & SYPH.]

A TREATMENT FOR PEDICULOSIS CAPITIS. WILLIAM A. DAVIS, J. A. M. A. 123:825 (Nov. 27) 1943.

A lotion containing 40 per cent of the monophenyl ether of ethylene glycol, 30 per cent of ethyl alcohol, 25 per cent of water and 5 per cent of methyl salicylate has proved to be satisfactory for the treatment of pediculosis capitis. This preparation rapidly kills lice and nits; it costs little, and it is not irritating.

HENSCHEL, Denver. [ARCH. DERMAT. & SYPH.]

MACRO- AND MICROGLANDULAR CASEATION IN PRIMARY TUBERCULOSIS IN CHILDREN. STEFEN ENGEL, Brit. J. Child. Dis. 40:104 (Oct.-Dec.) 1943.

A curve representing the age incidence of tuberculous meningitis reaches its peak in the second year. Tuberculous meningitis complicates a much higher percentage of the few tuberculous infections occurring in early childhood than of the many infections in later years.

In children up to 3 to 4 years the bronchial glands tend to be large, caseous and numerous. Not only are those glands which drain the site of the primary focus caseated, but also some or many others on the same side or on the other side. In older children the reverse is the case. The infection is confined to the regional glands in the majority of cases, and even these few glands remain small.

Early age gives rise to this particular type of glandular involvement, and this condition, again, may favor secondary spread. The author designates these two types of glandular response as macroglandular and microglandular caseation.

Tuberculous infection in young children is by no means always fatal. There may be a benign and a malignant form of primary tuberculosis.

There is the early period of infancy (up to the sixth or the eighth month), when almost invariably a fatal spread or gross pulmonary tuberculosis occurs. Thereafter comes the period of macroglandular response, up to the third or fourth year, the incidence decreasing as the age increases within this period. As soon as the child approaches school age the tendency to macroglandular tuberculosis diminishes and it occurs only exceptionally.

LANGMANN, New York.

DELAYED TUBERCULIN REACTION. MARC DANIELS, Lancet 2:600 (Nov. 13) 1943.

A number of persons who failed to react to either of the initial injections of tuberculin (0.1 cc. each of a 1:10,000 and a 1:100 dilution of old tuberculin) showed a reaction at the site of the last injection of tuberculin (1:100) several weeks after the initial tests. The reaction was of the same character as that of the reaction normally visible in positive reactors forty-eight to seventy-two hours after the injection of tuberculin.

It was assumed that the delayed reaction occurred shortly after an infection and that the reaction to tuberculin still present in the skin occurred at the time tuberculosensitivity reached a definite level.

The author propounds the question whether in these cases tuberculin was retained in the tissues in the absence of previous infection or the infection had occurred before the last injection of tuberculin and allergy had developed to a degree high enough for the antigen fraction of the tuberculin to be fixed intracellularly but not yet high enough to produce a typical reaction.

The author cites 14 instances of delayed reaction in persons who presented themselves for retesting six months after a previous negative reaction.

LANGMANN, New York.

Diseases of Blood, Heart and Blood Vessels and Spleen

ON THE CONSTITUTION OF PROTHROMBIN. ARMAND J. QUICK, Am. J. Physiol. 140:212 (Nov.) 1943.

Experimental findings are presented which indicate that prothrombin is composed of calcium and two other separate components, designated A and B. Component A disappears from oxalated plasma when the latter is stored in a refrigerator; it is presumably destroyed by oxidation. It is heat labile and to a certain degree group specific. In unmodified plasma it does not diminish, and therefore it can be concluded that component A when present in the intact prothrombin complex is stable. Component B disappears in the plasma of animals poisoned with dicoumarin (3,3'-methylenebis [4-hydroxycoumarin]). It is heat labile and is completely removed from oxalated plasma by aluminum hydroxide. This absorbent does not remove the factor from unmodified plasma; this indicates that when it is combined in the prothrombin complex it is not absorbed.

Views on the use of stored plasma for transfusion must be modified. Heretofore such plasma was considered unsuitable for treating hypoprothrombinemia. Since stored plasma loses only component A and as only component B is depleted in dicoumarin poisoning,

the employment of stored plasma should be as effective as that of fresh plasma.

At present all the cases of clinical hypoprothrombinemia appear to be caused by deficiencies of component B. Although depletion of component A has been observed only in vitro, it is entirely probable that clinical hypoprothrombinemia due to lack of this factor may occur.

NOURSE, Cleveland.

CONSTRUCTING DOUBLE AORTIC ARCH: REPORT OF A CASE. PETER A. HERBUT and THOMAS T. Smith, Arch. Otolaryng. **37**:558 (April) 1943.

A case of constricting double aortic arch incompatible with prolonged life is reported. A recognition that such a condition is possible, supplemented by a suitable roentgenographic study, offers diagnostic possibilities. It is hoped that a successful surgical procedure will be developed.

GREENWOOD, Chicago.

A CAUTION AGAINST TOO LIBERAL USE OF CITRATED BLOOD IN TRANSFUSIONS. JACQUES BRUNEAU and EVARTS A. GRAHAM, Arch. Surg. **47**:319 (Oct.) 1943.

In order to demonstrate that transfusions of blood treated with sodium citrate are not entirely innocuous when the material is injected in large quantities the authors carried on experimental transfusions in dogs, using citrated blood and heparinized blood. It was found that the dogs bled repeatedly and continually given transfusions of citrated blood survived a much shorter time than controls receiving heparinized blood. The difference seems to be due to the toxic action of large amounts of sodium citrate. The clinical application of these experimental results is difficult. The authors feel that it is impossible to establish the safe amount of citrated blood to be given in a certain period but do warn against the too liberal use of large amounts of citrated blood over a very short time.

KAISER, Rochester, N. Y.

TECHNIC OF INTRAVENOUS INJECTION IN INFANTS. MANDEL L. SPIVEK, Illinois M. J. **84**:323 (Nov.) 1943.

According to Spivek, giving a transfusion to an infant is not difficult if the method and apparatus used are subordinated to the successful insertion of the needle into the vein and maintenance of it there. Two technics are available: the less certain method of penetration of the skin and vein with a sharp needle and the more reliable method of exposure of the vein by dissection and insertion of a blunt needle. The first or sharp method appears to be the simpler of the two, but in actual practice it is the more difficult and frequently carries a higher percentage of failure. The percentage of failure varies directly with the skill and experience of the operator. The technics of the two methods are described in detail.

BARBOUR, Peoria, Ill.

INDICATIONS FOR BLOOD TRANSFUSION AND FOR THE INTRAVENOUS USE OF SALINE AND NUTRIENT SOLUTION. JAMES D. MCKINNEY, Illinois M. J. **84**:324 (Nov.) 1943.

The indications for blood transfusions are loss of whole blood or any of its constituents from the circulation, inability on the part of the body to supply

adequately the constituents of blood and need for stimulation or for the addition of immune substances. In considering the indications for the choice of saline solutions or of nutrient fluids one must consider the deficiency from which the child is suffering.

BARBOUR, Peoria, Ill.

CHLOROLEUKEMIA: REPORT OF A CASE. RAFAEL DE LA PORTILLA LAVASTIDA, Bol. Soc. cubana de pediatria **15**:121 (March) 1943.

The author reports a case of acute leukemia with painful symmetric chloroma-like masses in both lower extremities. Roentgenograms (which are not reproduced) revealed widespread periostitis and subperiosteal lesions resembling those seen in scurvy. The frequency of subleukemic and aleukemic varieties associated with chloroma is stressed, as is the importance of roentgenologic studies of bones in cases of leukemia.

KEITH, Rochester, Minn.

Diseases of Nose, Throat and Ear

EMOTIONAL DISTURBANCES FOLLOWING UPPER RESPIRATORY INFECTIONS IN CHILDREN. HELEN G. RICHTER, Am. J. Psychiat. **100**:387 (Nov.) 1943.

Between December 1940 and the time the report was written the author observed and treated 12 children with diffuse emotional disturbances that followed mild infections of the upper respiratory tract. In each case a supposedly normal child had suffered from an illness previously diagnosed as "flu," "grip," "cold" or "tonsillitis." The infectious phase was mild, and its duration was short, ranging from a few hours to a week. In each child there occurred a well defined change in personality within a month after the onset of the disease.

The emotional disturbances consisted of compulsive, obsessive, phobic thinking and behavior. The initial phase presented features similar to those of quasidelirium, motor restlessness, apprehension and lability of mood. The next phase was marked by heightened anxieties and a depressive mood with the apparent onset of compulsions and obsessions of various durations. Subsequently the children withdrew from their everyday interests. At first the withdrawal was from the less familiar and the more recently acquired expressions of socialization; later it was from the more superficial, interpersonal relationships and finally contact with familiar persons was severely disturbed.

The author stresses the importance of the type of personality of the child as a factor in these disturbances. In every instance the child was described as subservient, docile, cowed by authority, perfectionistic in his strivings and meticulous in his personal habits. The conforming attitudes masked underlying capacities for psychopathologic manifestations.

The author postulates that with illness hidden hostile and aggressive thoughts became manifest and dominant and the children attempted to cope with them by anancastic behavior. With psychotherapy these children reestablished themselves in their society with better adjustment than they had had prior to the onset of the illness.

JAHR, Omaha.

OSTEOMYELITIS OF THE SKULL RESULTING FROM INFECTION IN THE SINUSES. W. LIKELY SIMPSON, Arch. Otolaryng. **37:463** (April) 1943.

Eighteen illustrative cases are reported. The author recommends thorough removal of the primary focus of infection and wide removal of osteomyelitic bone as the best means of preventing complications such as meningitis and abscess of the brain.

GREENWOOD, Chicago.

LOCAL USE OF SULFATHIAZOLE FOR ACUTE PHARYNGEAL INFECTIONS. MARVIN S. FREEMAN, Arch. Otolaryng. **37:496** (April) 1943.

A study of 34 patients with acute infection of the pharynx or of the nasopharynx introduced a new method of locally treating the pharyngeal mucosa with sulfathiazole. The method rapidly produces subjective and objective relief and materially shortens the course of the disease. The possibility of systemic damage from the use of sulfathiazole is negligible with this method of treatment.

GREENWOOD, Chicago.

CLINICAL NOTES: A NEW METHOD FOR REMOVING WAX FROM THE EAR. FRANCIS L. WELLS, Arch. Otolaryng. **37:722** (May) 1943.

A new method for removing cerumen from the ear is the use of a metal suction tip with strong negative pressure; up to 25 pounds (11.3 Kg.) of suction may be used.

GREENWOOD, Chicago.

ACUTE AND CHRONIC MASTOIDITIS: CLINICAL ANALYSIS OF FIVE HUNDRED AND TWENTY-SIX CONSECUTIVE OPERATIONS. CHARLES EMORY TOWSON, Arch. Otolaryng. **38:32** (July) 1943.

A survey of 526 consecutive operations for acute and chronic mastoiditis is presented. Most of the operations for acute mastoiditis were performed during the second and fourth weeks of infection. Hemolytic streptococci were the predominant organisms, and most patients with acute mastoiditis had a leukocyte count of between 12,000 and 18,000. Cholesteatoma in nearly 50 per cent of the patients was found to be an indication for radical mastoidectomy. Of 205 patients with acute surgical mastoiditis, 98 per cent had dry ears; of 123 patients with radical mastoiditis, 90 per cent had dry ears. The residual hearing after radical operations was as good as the preoperative hearing or better in 63.8 per cent of the 94 patients for whom there were no follow-up records. The improvement apparently depended somewhat on the duration of otorrhea before operation but was independent of the healing time.

GREENWOOD, Chicago.

AN UNUSUAL NASAL TUMOR. BERT. E. ELLIS, Arch. Otolaryng. **38:65** (July) 1943.

An unusual type of adenocarcinoma in a 12 year old child is reported as cured with no recurrence after two years. The author believes that the area of such a tumor can be thoroughly cleaned without resulting extensive deformity by an external ethmoidectomy, a Caldwell-Luc operation and an intranasal operation combined. It is thought that the first procedure should be removal of the bulk of the tumor; at a second operation the base of the tumor may be more successfully cauterized, because of hemostasis.

GREENWOOD, Chicago.

LOCAL TREATMENT OF ACUTE RHINITIS WITH SULFATHIAZOLE. EVAN EBERT, Arch. Otolaryng. **38:324** (Oct.) 1943.

The author found that local treatment of acute rhinitis with insufflation of sulfathiazole proved effective, with no toxic effects of the drug and no complications. All age groups treated were between the ages of 1 and 81 years. However, it was felt that it is too early to draw any definite conclusion as to the value of therapy, because the number of patients thus far treated has not been large enough to justify conclusions.

GREENWOOD, Chicago.

ATRESIA OF THE EXTERNAL AUDITORY CANAL. LEE COHEN and SAMUEL FOX, Arch. Otolaryng. **38:338** (Oct.) 1943.

Acquired atresia (complete) of the external auditory canal is rare. Operative intervention is the only therapy, and the results are good. Congenital atresia of the external auditory canal occurs more frequently than is generally supposed. It is usually associated with microtia and other deformities of the external and the middle ear and therefore presents more problems. The unilateral type is best left alone, as the hearing is usually fairly good and operation at best offers only a moderate improvement in hearing and is usually attended by a poor cosmetic result. Patients with bilateral atresia should be operated on at an early age, because a handicapping loss of hearing is always present. It is the opinion of the authors that an operation analogous to the one described for traumatic atresia should be done rather than a radical mastoidectomy, as the latter is an unphysiologic attempt to convey sound waves to the middle ear and is attended by more risk than its uncertain results justify.

GREENWOOD, Chicago.

PATHWAY OF THE TONSILLAR LYMPHOCYTE. GEORGE KELEMEN, Arch. Otolaryng. **38:433** (Nov.) 1943.

The purpose of this article is to show the life history and ultimate fate of the tonsillar lymphocyte. The movements of the tonsillar lymphocyte represent in their entirety a passive transportation along preformed highways. The mobile elements in the germinal or action center are driven by increased intranodular pressure into the meshes of the reticulum. Portions of the reticulum penetrate into the layers of the epithelial cells. The projections of the reticulum carry the mobile elements within themselves. Increasing pressure causes these structures to expand and rupture the epithelium, so that the cells are conveyed into the lumen of the crypt. Here they are carried along threads of fibrin to reach the mouth of the crypt and are helped to reach the free surface of the tonsil by a tuftlike disposition of fibrinous fibrils. Changes in pressure initiated in the blood vessels of the capsule are responsible for formation of the secondary nodule and transportation of the mobile elements.

GREENWOOD, Chicago.

MUCOCELE OF THE FRONTAL SINUS: A REPORT OF FIVE CASES IN TWO OF WHICH AT OPERATION THE MUCOCELE WAS FOUND TO BE EMPTY. W. J. McNALLY, E. A. STUART and A. E. CHILDE, Arch. Otolaryng. **38:574** (Dec.) 1943.

An unusual circumstance in 5 cases of mucocele reported is that in 2 cases the mucocele was found empty at operation. There is no clinical method of determin-

ing without operation whether such a sinus is empty. Roentgenograms are a valuable adjunct in diagnosis. Photographs are presented.

GREENWOOD, Chicago.

MASTOIDITIS, MENINGITIS AND ABSCESS OF THE TEMPOROSPINOIDAL LOBE. LESTER L. CLEMAN, Arch. Otolaryng. **38**:590 (Dec.) 1943.

Described here is a case of mastoiditis, meningitis and abscess of the temporosphenoidal lobe. It illustrates the masking effects of sulfonamide compounds on otogenous infection and the surgical approach to the meninges by multiple incisions of the dura at the time of mastoidectomy. It further illustrates the value of sulfonamide compounds after the surgical focus has been adequately and thoroughly removed.

GREENWOOD, Chicago.

OTOSCLEROSIS IN IDENTICAL TWINS. HAERY C. ROSENBERGER, Arch. Otolaryng. **38**:594 (Dec.) 1943.

A report of identical twins with otosclerosis points to heredity as a factor.

GREENWOOD, Chicago.

PATULIN IN THE COMMON COLD: COLLABORATIVE RESEARCH ON A DERIVATIVE OF PENICILLIN PATULUM BAINIER. HAROLD RAISTRICK and others, Lancet **2**:625 (Nov. 20) 1943.

Patulin (a derivative of *Penicillium patulum* Bainier) was found to be about equally bacteriostatic to both gram-positive and gram-negative organisms. It was much less active than penicillin against gram-positive organisms but much more active against gram-negative organisms.

During four months patulin was given a trial in the treatment of common colds prevalent at a naval establishment. Solutions of the substance were sprayed in the nose or snuffed up from the hand. The results obtained were encouraging; 57 per cent of the treated patients recovered completely in forty-eight hours, compared with only 9.4 per cent of the controls.

LANGMANN, New York.

UPPER RESPIRATORY TRACT INFECTIONS. F. M. BURNET, M. J. Australia **2**:393 (Nov. 13) 1943.

Burnet presents an excellent discussion of infections of the upper respiratory tract. The material is considered under the following headings: (1) the etiology of the common infections of the respiratory tract, (2) the experimental study of influenza, (3) the recent incidence of influenza in Victorian camps, (4) the pathogenesis of influenza and (5) the control of infections of the respiratory tract. In the discussion of the last-mentioned aspect of the subject Burnet states that two pronouncements can be made. The first is that a large proportion of the winter respiratory and pharyngeal infections are not influenzal but are due partly to viruses not yet isolated and partly to bacterial pathogens. No immunologic approach to the control of these infections is yet possible. In the second place, it can be stated that in a clearcut epidemic of virus influenza, the evidence suggests that immunization of susceptible persons either by subcutaneous inoculations of formaldehyde-killed virus or by intranasal administration of living attenuated virus will reduce the incidence to a moderate degree; but no method has yet been conclusively proved to be effective, and the most that has been claimed is a 50 per cent reduction in morbidity. Such a moderate

degree of success may conceivably make it worth while to immunize large groups of persons engaged in important work, but it is hardly sufficient to suggest that immunization would be worthy of general application. Smorodintseff's report of protection of persons exposed to an epidemic by inhalation of immune serum in the form of a mist should be treated with reserve until the experiments have been repeated. It is not unlikely that some modification of his method may become the best practical means of protection against influenza in the midst of an epidemic. It is always possible that a specific chemotherapeutic agent will be discovered and will render all immunologic methods obsolete. If a pandemic of the 1918-1919 type should reappear, it will be a matter of major human importance to know whether the fatal outcome is essentially due to bacterial action and hence to be prevented by the use of sulfonamide drugs or whether the damage due to the virus is itself sufficient to cause death. In the latter circumstance no chemotherapeutic agent at present known would be of any value.

GONCE, Madison, Wis.

Diseases of Lungs, Pleura and Mediastinum

SUPPURATIVE ANTERIOR MEDIASTINITIS IN AN INFANT FOLLOWING INTRASTERNAL BLOOD TRANSFUSION. MARK M. RAVITCH Arch. Surg. **47**:250 (Sept.) 1943.

An 8 month old Negro girl after several infections was given an intravenous transfusion and several days later an intrasternal injection of blood. The following day there developed fever, dyspnea and obstruction to venous return of blood from the head, chest and arms, manifested by pronounced edema. Fluoroscopic examination showed a mass in the anterior mediastinum, overlying the base of the right ventricle. Aspiration of the mediastinum yielded pus. Recovery followed resection of the overlying sternum and costal cartilage. A discussion on the differential diagnosis of anterior and posterior mediastinitis follows.

KAISER, Rochester, N. Y.

ROENTGEN THERAPY OF INTERSTITIAL PNEUMONIA. ALBERT OPPENHEIMER, J. Pediat. **23**:534 (Nov.) 1943.

Interstitial pneumonia of children, characterized by infiltration around the bronchi and bronchioles without obstruction of the air passages and consequently without atelectasis, is akin to virus pneumonia of adults and does not seem to respond to the usual medical treatment. Good results were obtained by means of roentgen therapy with small doses and intermediate penetrations. Both the penetration and the individual roentgen dose must be adapted to the age of the child, the duration of the disease and sundry other factors. Doses exceeding 100 roentgens, given during the acute stages, resulted in severe constitutional reactions including chills and convulsions. No by-effects were observed with doses between 35 and 60 roentgens. As a rule, the clinical signs and symptoms subsided within one day or a few days after the first treatment, irrespective of the previous duration of the disease. Most of the patients received a single treatment.

OPPENHEIMER, Laconia, N. H.

THE COLD AGGLUTINATION TEST IN THE DIAGNOSIS OF PRIMARY ATYPICAL PNEUMONIA. GORDON MEYKLEJOHN, Proc. Soc. Exper. Biol. & Med. **54**:181 (Nov.) 1943.

Serums from 74 patients with primary atypical pneumonia and serums from 101 patients with various dis-

eases (pneumonia, mostly pneumococcic, tuberculosis, type A influenza, infection of the upper respiratory tract and lymphogranuloma venereum) as well as serum from 36 normal persons were tested for cold agglutinins. Sixty of the 74 patients with atypical pneumonia had titers of 20 or above, and three fifths of them had titers of 40 or above. The latter were considered definitely abnormal, as none of the patients from the control groups had titers which were greater than 20. During the first week only one fifth of the titers became positive, the rise began after eight to ten days of illness, reached a peak between the twelfth and the twenty-fifth day and fell off rapidly after the thirtieth day. There was no relation between the titer for cold agglutinins and the severity of the disease, but transmission of the infectious agent from patients with primary atypical pneumonia to cotton rats occurred most frequently from those whose blood contained cold agglutinins.

HANSEN, Minneapolis.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

FOREIGN BODY, JACKSTONE, IN THE ESOPHAGUS; PERFORATION; MEDIASTINITIS; RECOVERY. HARRY L. BAUM, Arch. Otolaryng. **38**:502 (Nov.) 1943.

This case illustrates the wisdom of leaving a foreign body in place in the esophagus for a time under special circumstances. The complication of esophageal perforation with mediastinitis and the eventual recovery without mediastinotomy are somewhat unusual. The case further demonstrates the fact that it is sometimes possible to withhold mediastinotomy and still achieve a successful result. External drainage was not necessary in this case—a fact which is not true in every case. Because of the fact that this patient's condition was favorable, it was not necessary to do mediastinotomy, and therefore that very serious procedure was avoided.

GREENWOOD, Chicago.

JEJUNAL INTUSSUSCEPTION. EDWIN PAUL SCOTT, J. Pediat. **23**:565 (Nov.) 1943.

Jejunal intussusception in a newborn infant is reported. An operation was performed on the sixth day of life, but the infant died on the seventh postoperative day.

This is believed to be the fourteenth instance reported of intussusception and the second of jejunal intussusception in a newborn infant.

SCOTT, Louisville, Ky.

DIAPHRAGMATIC HERNIA OF THE COLON IN AN INFANT WITH MONGOLISM. T. VALLEDOR and D. G. TEJERA, Bol. Soc. cubana de pediat. **15**:51 (Feb.) 1943.

A case of diaphragmatic hernia in a mongolian idiot aged 1 year is reported. The hernia was through the hiatus of Morgagni into the anterior mediastinum, and the authors feel that it was in part due to hypotonia of the diaphragm. Clinically the child had attacks of asphyxia and cyanosis, most marked in the supine position and at times accompanied by severe cough and fever. Roentgenologic examination showed that part of the transverse colon was in the right hemithorax.

KEITH, Rochester, Minn.

Nervous Diseases

ELECTROENCEPHALOGRAMS IN POST TRAUMATIC EPILEPSY: PRE-OPERATIVE AND POST-OPERATIVE STUDIES. HERBERT JASPER and WILDER PENFIELD, Am. J. Psychiat. **100**:365 (Nov.) 1943.

Jasper and Penfield present a general discussion of the problem of post-traumatic epilepsy and its differential diagnosis from essential epilepsy.

Eighty-six cases were analyzed with particular reference to the localization of the abnormal electrical discharges. Preoperative and postoperative studies were made on 32 patients on whom operations had been performed for the removal of epileptogenic lesions.

The electroencephalograms provide strong evidence that the technic of excision used by the authors is satisfactory. The gyri are completely, not partially, removed, and the pial covering of the remaining gyri is preserved.

JAHN, Omaha.

DIFFUSE LEUKOENCEPHALOPATHY WITHOUT SCLEROSIS. HERMAN JOSEPHY and BEN W. LICHTENSTEIN, Arch. Neurol. & Psychiat. **50**:575 (Nov.) 1943.

The authors described 2 cases of a progressive, deteriorative, fatal disease of the central nervous system in which there was diffuse leukoencephalopathy without sclerosis.

BEVERLY, Chicago.

RECOVERIES FROM STAPHYLOCOCCIC MENINGITIS FOLLOWING THERAPY. WARD J. MACNEAL, FRANCIS C. FRISBEE and ANNE BLEVINS, Arch. Otolaryng. **37**:507 (April) 1943.

The authors relate that in the ten years they have given to bacteriophage service there have been 11 recoveries from staphylococcic meningitis. The recovery may be achieved by the skilful use of bacteriophage without accessory therapy. However, this disease is in any case dangerous, and administration of a sulfonamide compound, especially sulfathiazole or sulfapyridine, is recommended with bacteriophage therapy. Eight clinical charts illustrate the article.

GREENWOOD, Chicago.

GUILLAIN-BARRÉ SYNDROME (ACUTE INFECTIVE POLYNEURITIS) WITH INCREASED INTRACRANIAL PRESSURE AND PAPILLEDEMA. F. R. FORD and F. B. WALSH, Bull. Johns Hopkins Hosp. **73**:391 (Nov.) 1943.

Two cases of this syndrome are reported in which, in addition to the characteristic features of the disease, increased intracranial pressure and papilledema were present. A review of the literature shows few references to papilledema in reports of acute infective polyneuritis.

LYTLE, New York.

THE GUILLAIN-BARRÉ SYNDROME. R. FINLEY GAYLE and DALE GROOM, J. Nerv. & Ment. Dis. **98**:488 (Nov.) 1943.

Gayle and Groom review briefly the literature and the characteristic clinical picture of the Guillain-Barré syndrome. They report the case of a 4 year old child in whom complete flaccid quadriplegia, paralysis of the left abducens nerve, distended bladder, generalized hyperesthesia and absence of deep reflexes appeared three or four days after apparent recovery from an

infection of the upper respiratory tract, in December 1942. A spinal tap on the fourth day in the hospital revealed 4 cells per cubic millimeter and a total protein content of 120 mg. per hundred cubic centimeters. Treatment according to the Kenny method was instituted, with local hot applications, manipulations, massage, exercises and use of removable casts. Recovery was progressive, and by September 1943 only some residual weakness and atrophy of the lower extremities remained. The authors believe the Kenny method to be of value in the treatment of this condition.

CHODOFF, Langley Field, Va.
[ARCH. NEUROL. & PSYCHIAT.]

PNEUMOCOCCAL MENINGITIS: RECOVERY FOLLOWING TREATMENT WITH SULFADIAZINE AND SPECIFIC ANTISERUM: REPORT OF A CASE. JAMES H. YOUNG, CHARLES SCHLOSBERG, CHARLES N. GETTES and SALVATORE A. MANCONI, New England J. Med. **229**:716 (Nov. 4) 1943.

Before chemotherapy became of common use, only in isolated instances was there recovery from pneumococcal meningitis. Prior to the use of the sulfonamide drugs mortalities as high as 95 to 100 per cent were reported. The few scattered recoveries reported may have been due to the use of specific antipneumococcus serum, alone or supplemented by various forms of drainage. With the advent of the newer chemotherapeutic agents the prognosis has become more promising. Some observers have found that the use of serum in combination with the sulfonamide drugs makes the outlook even better than when either is used alone.

A proved case of meningitis due to type V pneumococci with recovery is reported, with the plan of treatment outlined in detail. Both a chemotherapeutic agent and the specific antipneumococcus serum were employed. At no time did it appear advisable to institute surgical intervention on the mastoid.

GEGENBACH, Denver.

WATER-PITRESSIN TEST IN THE DIAGNOSIS OF EPILEPSY. HUGH G. GARLAND, A. PETER DICK and C. W. M. WHITTY, Lancet **2**:566 (Nov. 6) 1943.

For the purpose of diagnosis, fits can often be produced in persons with epilepsy by giving large quantities of fluid by mouth together with injections of pituitary extract containing pitressin. It is claimed that this procedure has never yet produced a fit in a person who is not epileptic. The test appears to be free from risk provided the patients are kept under close observation, are young and, apart from epilepsy, are healthy.

LANGMANN, New York.

TUBERCLES OF THE BRAIN IN THE COURSE OF DISSEMINATED PRIMARY INFECTION IN SMALL CHILDREN. T. VALLEDOR, Bol. Soc. cubana de pediat. **15**:105 (March) 1943.

Four cases of tubercles of the brain in small children are reported, in only 2 of which was the diagnosis confirmed by necropsy. In none of the cases did the spinal fluid show any changes except increase in pressure. The clinical signs were those of acutely increased intracranial pressure, such as vomiting, increased reflexes, positive Macewen's sign, headache and convulsions, but without definite changes in the ocular fundi or typical signs of meningitis.

KEITH, Rochester, Minn.

Psychology and Psychiatry

BREATH-HOLDING SPELLS. EDWARD M. BRIDGE, SAMUEL LIVINGSTON and CHRISTOPHER TIETZE, J. Pediat. **23**:539 (Nov.) 1943.

Breath-holding spells are common among small children. Calculations based on a study of 188 normal children who were brought to a well baby clinic showed an incidence of approximately 46 per cent. Most of such spells are of course mild and give little cause for concern to the parents. Among 95,000 children seen in the Johns Hopkins Hospital there were 83, or approximately 0.1 per cent, who presented breath-holding spells as a major complaint. Of this group of 83, 93 per cent showed cyanosis, 60 per cent unconsciousness and 49 per cent convulsions associated with the breath-holding spells.

Convulsions induced by breath-holding are distinguished from those due to epilepsy by means of a detailed description of the initiating circumstances. In the former, anger, pain or fear always precipitates crying and breath holding, which in time lead to cyanosis and convulsions. In epilepsy, precipitating circumstances are rare and crying, respiratory spasm, unconsciousness and convulsions begin almost simultaneously.

The background or cause of breath-holding spells involves a variety of factors. Parental mismanagement of the child and his habit training leading to episodes of violent anger and resentment is observed in a majority of these cases. In some, however, this is absent and the underlying difficulty appears to be an abnormal physiologic reactivity. In this group the attacks are commonly induced by pain rather than by anger or fear. Evidences of abnormal vagotonia may be observed in some children. Since the unconsciousness and convulsions associated with breath-holding spells are often related to the degree and duration of the cyanosis it seems likely that the mechanism involved is similar to that involved in the various forms of syncope, ordinary faints, carotid sinus sensitivity and paroxysmal heart block.

The great majority of children with breath-holding spells "outgrow" them before the end of the third year of life. In mentally retarded children, the spells tend to have a somewhat later age of onset and disappearance than in children with normal intelligence. A follow-up study was made of 41 of the 83 children who were brought to the hospital for breath-holding spells with the average age of almost 11 years. Approximately one third of the group showed behavior problems, but not more than would be expected in a similar group of normal children. Three children had convulsions unrelated to breath holding; 2 had typical epilepsy, and 2 others were suspected of having epilepsy, but the diagnosis could not be established.

BRIDGE, Baltimore.

Diseases of the Genitourinary Tract

URETERITIS: A CLINICAL SURVEY. DUNCAN M. MORISON, Edinburgh M. J. **50**:661 (Nov.) 1943.

The author states that ureteritis is not completely understood. He discusses the anatomy and physiology of the ureters, including the nerve supply, and the symptoms and causation of the disease. He divides the types of ureteritis into abdominal and pelvic groups as regards the clinical manifestations. The disease is clinically definite, though the pathologic changes and

the cause are not entirely clear. The lower end of the ureter is the site most frequently involved in both sexes. The condition occurs in children, but less commonly than in adults.

The treatment consists of ureteral dilation, short wave diathermy and denervation of the ureter.

NEFF, Kansas City, Mo.

Diseases of the Ductless Glands; Endocrinology

GROWTH OF THE HUMAN SUPRARENAL GLAND. C. A. SWINWARD, *Anat. Rec.* **87**:141 (Oct.) 1943.

At three months' gestation the medulla is less than 1 per cent of the total gland. At birth the medulla is 85 per cent of the cortex. The cortex degenerates in the first two weeks of postnatal life, so that the total gland decreases 50 per cent in size. The adult corticomedullary ratio is reached at 3 years of age.

SNELLING, Toronto, Canada.

STUDIES ON INACTIVATION OF ESTRADIOL BY THE LIVER. A. CANTAROW, K. E. PASCHKIS, A. E. RAKOFF and L. P. HANSEN, *Endocrinology* **33**:309 (Nov.) 1943.

It is generally believed that estrogens are rapidly inactivated by the liver, this belief being based largely on data obtained from four types of observation: 1. Hepatic tissue and cell-free extracts of liver have been found to inactivate estrogens in vitro. 2. It is reported that estrone is not inactivated when perfused through a heart-lung preparation but that it is rapidly inactivated when perfused through a heart-lung-liver preparation. 3. Ovaries transplanted to the mesentery or pellets of crystalline estrogen implanted in the spleen exert little or no estrogenic effect, as compared with the characteristic action of ovaries implanted subcutaneously; the same is true of estrogen injected into the spleen. 4. Enhancement of the effect of endogenous estrogen and of exogenous estrogens introduced into the systemic or portal circulations has been observed in animals and in human subjects with hepatic damage. However, the authors state the belief that critical analysis of the reported data reveals that the generally accepted views regarding the influence of the liver in this connection have been based on surprisingly few observations and that there are significant gaps and contradictions in the chain of evidence that forms the basis for these views.

They report experiments showing that little or no active estrogen can be recovered from the liver of a dog three to forty-eight hours after intravenous injection of 250,000 international units (2.5 mg.) of alpha estradiol. Twenty-four and forty-eight hours after injection of estradiol large amounts are present in bile from the gallbladder but none in the liver, spleen or intestinal wall or in blood from the hepatic vein. The livers of rats poisoned with carbon tetrachloride exhibit essentially the same capacity as the livers of normal rats for inactivating alpha estradiol in vitro. These observations do not support the hypothesis that the increased activity of endogenous and exogenous estrogen in the presence of hepatic damage is due to decreased inactivation of estrogen by the damaged hepatic cells.

The following hypothesis is offered as being in accord with all available data: Estrogen is removed from the blood by the hepatic cells, converted to a substance possessing little or no estrogenic activity, in part stored temporarily in the liver in this form and "reactivated"

during the process of its excretion by the hepatic cells. Estrogen probably undergoes an enterohepatic circulation similar to that of bile acids, being, perhaps, gradually destroyed or converted to a permanently inactive substance.

JACOBSEN, Buffalo.

EFFECT OF ADRENAL CORTICAL COMPOUNDS ON LACTATION. WARREN O. NELSON, ROBERT GAUNT and MALVINA SCHWEIZER, *Endocrinology* **33**:325 (Nov.) 1943.

Further evidence is presented of the important role played by the adrenal cortex in the initiation and maintenance of lactation. Potent preparations of lactogenic hormone are powerless to induce the secretion of milk in hypophysectomized guinea pigs unless aided by the action of adrenal substance. This aid may be provided with equal effectiveness in the form of hormone produced in the adrenal cortex as the result of stimulation by the adrenotropic factor or directly as adrenal cortex extract supplied by injection. These substances probably act, in part at least, through mechanisms involving both of the well known functions of the adrenal cortex, the actions on salt and water and on metabolism of carbohydrates.

Substances which promote mammary growth in general inhibit lactation. Thus estrogen, a potent stimulant to the growth of the mammary gland, inhibits secretion of milk. The same appears to be true, although from a quantitative standpoint to a lesser degree, of desoxycorticosterone. Such inhibition is probably effected in the hypophysectomized animal by a direct action on the mammary gland and in the normal animal by an effect on the hypophysis as well as on the mammary gland.

JACOBSON, Buffalo.

ENDOCRINE AND PSEUDOENDOCRINE PROBLEMS IN CHILDHOOD. RICHARD WAGNER, *New England J. Med.* **229**:737 (Nov. 11) 1943.

Rightfully, endocrine and pseudoendocrine problems in childhood deserve consideration together. Many anomalies and disturbances of growth and development and certain instances of retarded sexual development, abnormal accumulation and distribution of fat, dwarfism and even mental retardation are often mistakenly grouped as expressions of endocrine imbalance.

There are three large groups of diseases and anomalies that have certain features in common but that differ from each other in causation and in the dominance of certain characteristics. Group 1 includes the true endocrine disorders caused by pathologic processes or by anomalies of endocrine glands, including congenital absence. Group 2 includes the accentuations of physiologic phases of development, which sometimes imitate true endocrinopathies. Constitutional and familial factors are frequently involved. Temporary states such as transitory infantilism, certain forms of obesity and disharmonic development should be included. Group 3 includes congenital anomalies and multiple deviations and retardation of development, somatic as well as mental, sometimes mistaken for endocrinopathies, and showing some of their essential features. Not infrequently they overlap. Conditions in this group should properly be called genopathies rather than endocrinopathies.

In the physical examination of children with endocrine or pseudoendocrine disturbances special attention should be given to hematologic studies (hypochromic anemia occurs in myxedema), the heart and electrocardiogram (characteristic changes are present in hyperthyroidism and hypothyroidism), the blood pressure (elevation

occurs in adrenocortical obesity with macrogenitosomia) and the size of the liver (hepatomegaly is present in dwarfism due to glycogenosis).

GENGENBACH, Denver.

Diseases of the Eye

SWIMMING-BATH CONJUNCTIVITIS, WITH A REPORT OF THREE PROBABLE CASES AND A NOTE ON ITS EPIDEMIOLOGY. E. H. DERRICK, M. J. Australia **2**:334 (Oct. 23) 1943.

The author reports 3 cases in which inclusion blennorrhoea appeared six to seven days after simultaneous exposure of the patients in a swimming pool. In all 3 patients the conjunctivitis was accompanied by severe constitutional symptoms which persisted for five days.

GONCE, Madison, Wis.

Skin Diseases; Allergy

TREATMENT OF TINEA WITH ETHYL CHLORIDE. NATHAN BOGRAD, Arch. Dermat. & Syph. **48**:511 (Nov.) 1943.

The author has found that the method described gives uniformly excellent results, and he has found no contraindications for its use. Ethyl chloride is sprayed on the lesion until the temperature of the skin is lowered sufficiently to produce a white surface. Primary lesions or small grouped lesions with no erythema are sprayed a few seconds longer. If the lesion is a vesicle, the spray is applied to the whole area; if it is a macule or a larger lesion, the spray is applied around the edge, and two to four applications are made, depending on the size. Distant allergic manifestations require only one application to allay itching.

JACKSON, Iowa City.

AN APPRAISAL OF THE PRESENT STATUS OF PROPHYLAXIS AGAINST POISON IVY. FRANCIS A. ELLIS, J. Allergy **14**:557 (Nov.) 1943.

The author reviews the present status of prophylaxis against poison ivy and reports his experience with the use of tablets containing an ethereal extract of poison ivy for 5 patients. Immunity to poison ivy developed in these patients. Pruritus ani, which is an annoying reaction to the treatment, can be relieved by watching the dose and by allowing rest periods during the treatment.

HOYER, Cincinnati.

THE TREATMENT OF WARTS. ARTHUR BURROWS, Brit. J. Dermat. **55**:60 (March) 1943.

The author states that the chief methods of treatment of warts are: (1) general (internal medication and psychotherapy); (2) use of local keratolytics (glacial acetic acid and salicylic acid); (3) use of cautery, diathermy (electrocoagulation) or solid carbon dioxide (the author prefers cautery because of the better cosmetic appearance afterward); (4) excision and curettage (according to the author one of the most satisfactory methods of dealing with warts), and (5) radiologic methods, which include (a) superficial irradiation (unscreened or lightly screened rays with a kilovoltage of 80 to 100); (b) the Chaoul technic (contact or close therapy with a kilovoltage of about 60); (c) grenz rays emitted at about 10 kilovolts, and (d) radium.

BLUEFARB, Chicago. [ARCH. DERMAT. & SYPH.]

Miscellaneous

PENICILLIN AS A CHEMOTHERAPEUTIC AGENT. MARTIN H. DAWSON, GLADYS L. HOBBY, KARL MEYER and ELEANOR CHAFFEE, Ann. Int. Med. **19**:707 (Nov.) 1943.

Penicillin exhibited strong antibacterial action against gram-positive organisms and against gonococci and meningococci. It was not effective against other gram-negative bacteria. Its action is both bactericidal and bacteriostatic. It is effective in the presence of pus and inflammatory exudates. Penicillin is nontoxic in much larger doses than are necessary therapeutically.

READING, Galveston, Texas.

THE PHYSIOLOGICAL BASIS OF PARENTERAL FLUID ADMINISTRATION. DONALD E. CASSELS, Illinois M. J. **84**:320 (Nov.) 1943.

The blood volume of a normal child is 85 to 90 cc. per kilogram of body weight; it is increased in malnutrition and in edema and is decreased in obesity and in dehydration. The volume in infants is low when related to surface area.

The volume of blood is easily reduced by illness, especially when there is vomiting or diarrhea, and the reduction interferes with the renal control of the acid-base balance.

While the volume of body fluid may be measured by laboratory methods, clinical estimation of dehydration continues to be difficult. The weight changes with the volume of body fluid and this change and the clinical appearance continue to be the only bedside criteria of dehydration available at present.

The volume necessary for normal circulation and renal function and the content of electrolytes may be restored by parenteral administration of isotonic solution of sodium chloride with 5 per cent dextrose. The necessary amount may best be judged by the maintenance of weight, by the maintenance of moisture in the mouth and, best of all, by the maintenance of urinary output.

In circulatory failure or distress subcutaneous fluid is not readily absorbed, and when fluid is administered intravenously to persons with circulatory distress it is wise to follow the venous pressure, which may be done simply.

BARBOUR, Peoria, Ill.

THE PARENTERAL ADMINISTRATION OF VARIOUS THERAPEUTIC AGENTS. ORVILLE BARBOUR and ROBERT D. HART, Illinois M. J. **84**:326 (Nov.) 1943.

This paper is a résumé of the useful and dependable types of parenteral therapy. The generally accepted indications for this therapy, the interpretations of the results and the methods commonly used in the administration of the various types of therapeutic agents are outlined. The intradermal, subcutaneous, intramuscular, intravenous and intraspinal routes of medication as used by the pediatrician are each discussed.

BARBOUR, Peoria, Ill.

MICROBIOLOGICAL ASPECTS OF PENICILLIN: I. METHODS OF ASSAY. JACKSON W. FOSTER and H. BOYD WOODRUFF, J. Bact. **46**:187 (Aug.) 1943.

One of the most pressing issues confronting workers engaged in studies of penicillin is the matter of establishing with some degree of certainty and accuracy the

potency of solutions of penicillin. Wide divergencies in methods of assay now exist. The authors have attempted to compare the different types of assays. They recommend that unknowns be tested daily with a standard preparation of penicillin of known Florey unitage to minimize uncontrollable fluctuations. Serial dilution methods, with liquid or solid mediums, are wanting in accuracy and do not yield specific values for penicillin activity. A modified broth method devised in the Squibb laboratories gives good sensitivity and is practical. The turbidimetric method has application in special types of investigations in which high accuracy is required, but it is too difficult for routine assays. The Oxford cup method (modified) is an excellent method for routine assays, especially for large numbers of samples. The article should be consulted for the details of the experiments characterizing the different methods.

STOESSER, Minneapolis.

MICROBIOLOGICAL ASPECTS OF PENICILLIN: III. PRODUCTION OF PENICILLIN IN SURFACE CULTURES OF *PENICILLIUM NOTATUM*. J. W. FOSTER, H. B. WOODRUFF and L. E. MCDANIEL, *J. Bact.* **46**:421 (Nov.) 1943.

Realizing that an increased interest in penicillin as a chemotherapeutic agent would lead to a greater demand for the product, the authors made an extensive investigation of the production of this substance. They found that different strains of *Penicillium notatum* vary widely in the ability to produce penicillin and that the selection of the most potent strains is of primary importance for maximum production. Furthermore, active strains tend to degenerate or lose their capacity to produce penicillin, especially after continued serial transfer on laboratory mediums. This degeneration can be eliminated by reducing the number of vegetative transfers as described by the authors. Active cultures when plated yield isolates with different degrees of penicillin activity. Penicillin is produced when the pH of the medium does not fall to lower than 4 during the early stages of growth of the culture and in the later stages rises rapidly to 6.0 to 8.5. The presence of traces of certain elements, notably zinc, and also of organic supplements, favors the rapid rise in pH and the formation of penicillin. Zinc in particular acts in this manner by catalyzing the complete oxidation and utilization of dextrose by the mold, thus preventing the accumulation of gluconic acid which is responsible for the fall in pH of the medium.

STOESSER, Minneapolis.

AN "IMPROVED" CONSULTANT'S CASE FOR PEDIATRIC PHYSICIANS. R. A. WILSON, *J. Pediat.* **23**:568 (Nov.) 1943.

An improved case for pediatric physicians is described. The case itself is of rigid leather "brief case" construction. The lid will fasten open at an angle of 90 degrees. The main compartment is subdivided to hold diagnostic instruments for the ear, a sphygmomanometer, hemoglobinometer and stethoscope. There are also spaces for containers for antiseptics, dressings and drugs. The inner side of the lid holds a pen, pencil and pen light

as well as prescription and memoranda pads. The outer side of the lid has bellows type leather compartments to carry the numerous insurance papers, history forms and diet sheets which modern pediatric practice requires. The case is described as functional rather than traditional.

WILSON, Winnipeg, Manitoba, Canada.

EFFECT OF ORAL ADMINISTRATION OF SUCCINYL SULFAPYRAZINE ON BACTERIAL (COLIFORM) FLORA OF THE INTESTINE OF NORMAL MICE. FRITZ T. CALLOMON, *J. Pharmacol. & Exper. Therap.* **79**:200 (Nov.) 1943.

It was found that succinyl sulfapyrazine "proved highly effective and at least equal to sulfaquandine in diminishing the density of coliform bacteria in the contents of the intestine of normal mice." Succinyl sulfapyrazine was more effective than sulfasuxidine (succinyl sulfathiazole), and the toxicity was low when the drug was fed to mice in large quantities.

PILCHER, Cleveland.

ON THE MECHANISM OF FEVER PRODUCTION WITH INFLAMMATION. VALY MENKIN, *Proc. Soc. Exper. Biol. & Med.* **54**:184 (Nov.) 1943.

In a study of the production of fever by inflammatory reaction fractionization of exudates was made and the various fractions were injected intracardiacally into dogs. The only fraction which produced a fever in these animals was the euglobulin fraction, called necrosin. Hyperthermia was not induced by injection of other protein fractions derived from ascitic fluid or normal blood serum or by injection of other fractions of exudates. At present the mechanism by which necrosin produces the febrile response is not known.

HANSEN, Minneapolis.

ACTINOTHERAPY IN CHILDREN. EVA MORTON, *Brit. J. Child. Dis.* **40**:68 (July-Sept.) 1943.

The types of apparatus used were the centrosol lamp for collective irradiation, the duotherapy units and the Kromayer lamp. A course consisted of three months' treatment with two sessions weekly.

Rickets and debility were the commonest reasons for referring infants and young children to the actinotherapy department. Others were malnutrition, adenitis, alopecia, psoriasis and other cutaneous diseases. Regular attendance for not less than twenty treatments was almost indispensable for cure of most of these conditions.

LANGMANN, New York.

CHANGING VIEWS ON DIGITALIS. EDITORIAL, *Edinburgh M. J.* **50**:687 (Nov.) 1943.

The name of the author of this editorial is not mentioned. The writer briefly reviews the historical contributions to the subject beginning with that of Withering in 1785 and devotes a few lines to each of the many contributors in sequence since the time of Withering. With regard to digitalis therapy for children, he quotes Sutherland, who reported in 1919 that digitalis specifically slows the rapid hearts of rheumatic children if the rhythm is normal; it does not act as a cardiac tonic but merely serves as a check to an increased rate.

NEFF, Kansas City, Mo.

Society Transactions

AMERICAN PEDIATRIC SOCIETY

JAMES L. GAMBLE, M.D., *President*

HUGH McCULLOCH, M.D., *Secretary*

*Fifty-Fifth Annual Meeting, Atlantic City, N. J.,
Sept. 26-27, 1944*

First Session

Tuesday Afternoon, Sept. 26

President's Address. DR. JAMES L. GAMBLE, Boston.

This paper will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

Intestinal Alkalosis. DR. DANIEL C. DARROW, New Haven, Conn.

A report is made of a new syndrome. The patient showed intractable watery diarrhea from birth to the time of this report (age 2 years and 7 months). The stools were acid and contained considerable amounts of sodium, chloride and, at times, potassium. The alkaline urine contained no chloride, little sodium, and varying amounts of potassium. The stool chloride was always greater in amount than the stool sodium, and the stool water was greater than the urine water. The absorption of nitrogen, fat, carbohydrate, phosphorus and calcium was essentially normal. As a result of the disturbances mentioned, the boy grew slowly and was subject to frequent exacerbations of the diarrhea accompanied by signs and symptoms of dehydration. The blood serum showed extreme alkalosis, the maximal values being: pH 7.73; bicarbonate, 47 millimols per liter; chloride, 45 millimols per liter; sodium, 118 millimols per liter. Occasionally, the serum potassium was low (1.5 millimols per liter), but usually it was normal. Usually no signs of tetany were present, but tetanic convulsions occurred once and carpopedal spasm occasionally.

Metabolic data are presented which show that, as chloride is lost more rapidly than sodium, extracellular sodium is transferred into intracellular fluids and approximately equivalent amounts of potassium are released from the cells and excreted. Similarly, when dehydration is treated with sodium chloride and potassium chloride, insufficient sodium is retained to account for the expansion of extracellular chloride, but retention of potassium accounts for the release of sufficient sodium from cells to explain the changes in extracellular electrolytes.

DISCUSSION

DR. IRVINE McQUARRIE, Minneapolis: The 2 cases reported independently by Drs. Gamble and Darrow undoubtedly represent a heretofore undescribed clinical entity appropriately referred to as intestinal alkalosis. Now that the existence of such an entity has been demonstrated, similar cases will probably be discovered more frequently than when they were not being looked for. It would be most interesting to know the nature of the mechanism involved in the excessive loss of chloride in the diarrheal stools in these unusual cases. Since Dr. Gamble has ruled out the presence of aberrant

gastric mucosa in the colon as a cause, the peculiar disturbance described suggests an analogy with certain renal abnormalities in which impairment of function is due entirely to failure of tubular reabsorption.

The Nature of Some Diseases Ascribed to Disorders of Lipid Metabolism. DR. SIDNEY FARBER, Boston.

The important contributions of Rowland, Pick and others led to what appeared to be a rational classification of diseases of lipid metabolism. These included Gaucher's disease, Niemann-Pick disease and Hand-Schüller-Christian disease, which were thought to be differentiated by disturbances of kerafin, sphingomyelin and cholesterol metabolism respectively.

Experience with these conditions accumulated in recent years necessitates a reconsideration of their nature and interrelationships and of the nomenclature employed. The error in lipid metabolism in Gaucher's disease is related closely to that in Niemann-Pick disease (Thannhauser). Recent chemical and pathologic studies give further proof that these two diseases are disorders of lipid metabolism and are probably of intracellular origin. There is no evidence to support the conception of "storage" disease. Eponyms are preferable to misnomers such as xanthomatosis and reticuloendotheliosis. Niemann-Pick disease, for example, is far more than a disturbance of the reticuloendothelial system: Many different organs and types of cells may be involved. The original observation as to a predilection on the part of diseases of lipid metabolism for the Jewish race is not supported by recent experience. The period of survival in Niemann-Pick disease may be much greater than the twenty-seven month maximum reported in the literature: I have studied tissue from 2 patients with Niemann-Pick disease, and these patients are still alive, 1 at the age of 6 years and the other at 10 years.

Hand-Schüller-Christian disease, originally considered a disturbance of cholesterol metabolism characterized by the triad of bone and eye involvement and diabetes insipidus, is now regarded as a slowly progressing chronic form of a disease the pathologic result of which may be either fibrosis or accumulation of masses of cholesterol-laden phagocytes in many parts of the body. The early lesions are granulomatous and bear little resemblance to the end stage, which was responsible for the term "xanthoma." The recent suggestion by Wallgren that Letterer-Siwe disease is only a more severe and acute form of Hand-Schüller-Christian disease receives further support. Experience has strengthened my suggestion that the solitary or multiple destructive lesion of bone called by Jaffe and Lichtenstein eosinophilic granuloma of bone is but a variation of the basic process of which Hand-Schüller-Christian and Letterer-Siwe disease are other examples. Studies of all three conditions lead to the following conclusions: 1. These are all variations of the same disease, with the clinical picture dependent on the sites involved and the rapidity of the course. 2. Lipid, when present, is liberated as a part of the local destructive inflammatory process. 3. There is no evidence that these diseases represent errors of lipid metabolism. There is no justification, therefore, for classifying these diseases

with Gaucher's disease and Niemann-Pick disease. 4. A satisfactory working classification of these conditions should include the three separate clinical types of Hand-Schüller-Christian disease, Letterer-Siwe disease and eosinophilic granuloma of bone, with transitional forms between eosinophilic granuloma and each of the other two diseases in this group. 5. These conditions are probably of infectious origin. When the exact cause is discovered, the cumbersome nomenclature now employed should be dropped.

DISCUSSION

DR. ALFRED HAND, Philadelphia: I wish to give my best thanks to Dr. Farber for taking up this study of lipid metabolism and for the valuable points he has made. I hope that he will continue his research until he has made the whole problem of lipid granulomatosis perfectly clear, for I think it is the most important field for investigation not only in pediatrics but in internal medicine. I may be biased in my judgment because of my special interest in it, which started during my internship the first year after my graduation. I then showed that I knew less than nothing about lipid granulomatosis by erroneously describing it in my first case as tuberculosis with polyuria. Now I know a few facts about it, but they point to many unanswered questions.

I am glad to be able to show you a slide from the liver of the patient in that case. Neither the able demonstrator of pathology, Dr. W. S. Carter, who assisted me at the autopsy and who made the histologic studies, nor the professor of pathology, Dr. George Gustave Guiteras, could explain the lesions. You may save to take my word that that is liver, so great is the regeneration of the parenchyma with infiltration of small round cells, histiocytic foam cells and some multinucleated giant cells.

The next slide is from the patient in my second case, which I reported to the society twenty-four years ago; perhaps the ten active members of the society who were present then will recall the photographic print of the roentgenogram, but I am sure they as well as some others of you will be interested in comparing this slide with the next one, which shows the patient ten years later, and noting the restoration of normal bone in the large areas that were completely devoid of it. It was most marvelous and unexplained recovery. In the spring of 1943 that young man was a patient in the Army hospital at Camp Van Doren, Miss.

The final slide is from a lipid granuloma which formed in the right lower eyelid of my third patient, whom I have been studying now for three years in the children's ward of the Methodist Hospital through the kindness of my colleagues, Dr. John Diven, the pediatrician of the hospital, and his assistant, Dr. Muldawer. For the first seventeen months after his admission to the hospital the patient showed no improvement, his weight remaining stationary at about 20 pounds (10 Kg.). Then a gain in weight set in, which has continued for these two years, so that he now weighs 43 pounds (19.5 Kg.) at 5½ years of age. Pitressin tannate in oil keeps down thirst and polyuria for several days at a time, and he is now attending school, showing bright mentality.

DR. ARILD E. HANSEN, Galveston, Texas: May I ask Dr. Farber whether the deposition of cholesterol esters in the tissues in the so-called generalized type and also in the eosinophilic granuloma type was different from or similar to that in Hand-Schüller-Christian disease?

It so happens that at the University of Minnesota I had 2 patients recently with the generalized type, and

in these children I found that very late in the disease there was a disappearance of cholesterol esters from the blood stream. The value for this dropped to 36 mg. in 1 of them and to 2 mg., or almost a negligible amount, in the other.

Analysis of the tissues in these children has not been completed as yet, but preliminary studies of the affected bone marrow show an increase in the cholesterol ester fatty acids to about 4,000 times the level found in normal bone marrow.

DR. BENJAMIN KRAMER, Brooklyn: I wonder whether the patients with Niemann-Pick disease that Dr. Farber referred to showed any evidence of mental retardation or any abnormalities in the retina.

DR. SIDNEY FARBER, Boston: Both are slightly retarded.

Clinical and Blood Lipid Studies in a Child with Chylous Ascites. DR. ARILD E. HANSEN and HILDA F. WIESE, PH.D. (by invitation), Galveston, Texas.

An unusual opportunity to study the clinical and metabolic effect in a human subject of prolonged use of a diet extremely low in fat was afforded when a 3 week old boy was found to have chylous ascites. After removal of the creamy fluid, which relieved the respiratory distress of the patient, he was placed on a regimen which was believed to be nutritionally adequate except for fat. The total consumption of fat for the first year or so was calculated to be in the neighborhood of 1 Gm. daily. In addition to periodic clinical observations, determinations of the lipids of the serum, the ascitic fluid and the mother's milk were made.

As regards the clinical observations, the following points were noted: 1. Gain in weight appeared to be fairly satisfactory during the first year, but periodic removal of ascitic fluid made difficult the interpretation of gain in weight. On the other hand, increase in height was satisfactory. 2. No abnormality was observed as regards the routine examinations of the blood and the urine other than a tendency of the hemoglobin to be slightly low. 3. For the first few months the number of stools was greater than normal, and there were several attacks of diarrhea. 4. The child experienced severe reactions to infections of the upper respiratory tract, five such episodes having been observed. 5. The most marked clinical effects were referable to the skin. Impetigo was very resistant to treatment. Prickly heat was extensive during the hot weather, and the eruption persisted months after the onset of cool weather and long after the skin of other children so affected had cleared. Also, when he was about 6 months of age eczematous patches developed on the cheek, the scalp and various other parts of the body. These lesions responded readily to treatment. 6. When he was examined at the age of 15 months, his appearance was not that of a healthy, robust child. Although the abdomen was large, he was active and was able to walk with assistance.

Determination of the serum lipids, including the fatty acids, such as glyceride, phospholipid and cholesterol ester, revealed an abnormally low degree of unsaturation in all fractions. This result suggested that the infant was unable to synthesize highly unsaturated fatty acids. Administration on two occasions of a cream meal with a study of the serum lipids four and five hours later revealed no evidence of absorption of fat directly into the blood stream. That all dietary fat was absorbed from the intestine into the lymph channels was further evidenced by the fact that the average

molecular weight and the average iodine number of the fatty acids in the mother's milk (256 and 54.6 respectively) and in the ascitic fluid (254 and 56.7 respectively), determined when the child was 3 weeks old, were practically identical. Both the vitamin A and the carotene existed in higher concentration in the ascitic fluid than in the serum.

I hope to obtain consent of the parents to an operation effecting communication of the internal saphenous vein to the peritoneal cavity.

The Biosynthesis of B Vitamins in Man. DR. L. EMMETT HOLT JR. and DR. VICTOR A. NAJJAR (by invitation), Baltimore.

The bacterial synthesis of B vitamins has been demonstrated in fowls, in the rumen of ruminant animals and, under certain conditions, in the cecum of the rat, but no information has been available as to its occurrence in human beings. We encountered this phenomenon in the course of some experiments designed to elucidate the requirements of human beings for various B factors. Experimental subjects were fed a synthetic diet in which the B factors were supplied as pure substances in accurately measured quantities. A gradual reduction of the intake of thiamine led to symptoms of thiamine deficiency in some subjects but not in others. Failure to show symptoms could be correlated with the presence of considerable quantities of free thiamine in the stools. In some subjects the excretion of thiamine by this route was consistently higher than the intake. That this stool thiamine was produced by intestinal bacteria was shown by the fact that it could be made to disappear by administration of succinylsulfathiazole. The intestinal synthesis of thiamine afforded only partial protection against thiamine deficiency, for with a minimum intake of thiamine it eventually failed and in all but 1 of 9 subjects deficiency symptoms developed. This result suggests that some thiamine is required for the nutrition of the bacteria that produce thiamine.

In a second series of experiments the intake of riboflavin was reduced to between 70 and 90 micrograms per day. With this intake the daily output of riboflavin in the stools was sustained for six weeks at a level from four to ten times the intake. The administration of succinylsulfathiazole for an additional five weeks caused no appreciable decrease in the excretion of riboflavin, a result which indicates that this factor can be produced by bacteria which are resistant to the drug. No symptoms of riboflavin deficiency were observed during the experimental period.

The observation that intestinal bacteria may synthesize B vitamins carries implications important for human nutrition. It indicates that under certain conditions at least the commonly accepted requirements for these factors are far too high and that a factor of safety exists which has not hitherto been appreciated. The conditions which influence this biosynthesis remain to be accurately defined.

Comparison of the Effect of Vitamin D and Citrates on Mineral Metabolism in Late Rickets. DR. LASLO KAJDI, Baltimore.

Two brothers, 8 and 6 years old respectively, with rickets were studied. Both have received the usual amounts of vitamin D but have had little exposure to sunshine. The rachitic deformities were mainly restricted to the lower extremities. Physical examination showed no other abnormalities. Roentgen examination indicated active rickets. With respect to the chemistry of the blood, a low level of serum phosphorus (3.2 and

2.6 mg. per hundred cubic centimeters of blood) and increased phosphatase activity were the only abnormal findings. The nonprotein nitrogen and the carbon dioxide-combining power were normal. The test for tolerance of dextrose and the test for renal function gave normal results. Examination of the urine gave normal results. No excessive excretion of organic acid was found. On administration of ammonium chloride the patients were able to excrete acid urine.

On studies of the calcium and phosphorus balance made before treatment was begun, it was found that both with low and with normal intake of calcium and phosphorus the patients had a negative balance of calcium and to a less degree of phosphorus. The excretion of urinary calcium was extremely low; the urinary-fecal phosphorus partition was also low, though to a less degree this abnormal partition was independent of intake. Therapy both by means of citrates and by administration of vitamin D significantly improved the mineral balance. The level of urinary calcium increased. The levels of fecal calcium and phosphorus diminished, a fact which indicates better absorption. While the vitamin D did not affect significantly the level of phosphates in the urine, the citrate increased it to about 25 per cent above the level during the control period. One hundred cubic centimeters of molar citrate solution produced results comparable to those given by 10,000 U. S. P. units of vitamin D.

In spite of these favorable changes in metabolism roentgen examination did not indicate healing under either regimen during a period of two months. Therefore both children were given large doses of vitamin D—50,000 and 200,000 U. S. P. units respectively—resulting in further improvement in the mineral metabolism and roentgenographic evidence of healing in two months and three weeks respectively. The serum phosphorus and the phosphatase activity were little affected by the vitamin D, even in these massive doses, while administration of citrates actually decreased both the serum calcium and the serum phosphorus. Studies of the urinary clearance of mannitol and phosphorus indicated normal glomerular filtration and high phosphate clearances. Both therapeutic measures decreased the phosphate clearances and thus moderately improved the tubular reabsorption of phosphate.

After corrective osteotomy while in cast a high level of serum calcium and abnormally high excretion of urinary calcium were observed, in spite of the vitamin intake's having been reduced by one third. Administration of the vitamin was discontinued for twelve days. Thereafter 60,000 U. S. P. units kept the patients in satisfactory condition. After removal of the cast and the resumption of normal activities a less favorable balance was obtained. The level of serum phosphorus diminished; nevertheless, roentgenograms indicated further healing.

The healing of vitamin D-resistant rickets without significant rise in the level of serum phosphorus has been observed by previous investigators also.

DISCUSSION

DR. ALLAN M. BUTLER, Boston: I think it might be desirable to supplement Dr. Kajdi's findings about the effect of operation on patients with late resistant rickets by such findings as Dr. Green and I have had in the treatment of a series of patients, because one should be aware of what may happen when one operates on such a child.

We have had 3 children who had osteotomies and who had persistent rickets for years; the rickets had been only partially controlled by the giving of hundreds

of thousands of U. S. P. units of vitamin D a day. The first child was brought in for operation, and her usual dose of 100,000 U. S. P. units of vitamin D was given up to the day of operation. Shortly after operation, it was noted that the child had hematuria. Examination of the urine showed calcium phosphate casts. The serum calcium and the inorganic phosphates were elevated above normal. The level of the serum phosphatase had fallen. Thus the child's blood chemistry had undergone such a change as would not only lead to complete healing of the rickets but also to an increase in the product, serum calcium times serum phosphorus, that resulted in serious hematuria.

Roentgenograms taken at that time showed that the rickets, which we for years had been unable to heal completely by administering large doses of vitamin D, was well healed.

When we operated on the other 2 children, we discontinued the administration of vitamin D for, I think, approximately a week before the operation. These 2 children had the same abnormal rise in serum calcium, with elevation of the serum inorganic phosphorus to a normal level and dropping of phosphatase to normal. Roentgenograms also showed complete healing of the rickets.

Therefore, we have these cases to add to those which Dr. Kajdi has just reported. Our experience makes us very careful of the urine volume of such children after operation.

We have also had some other complications. I see that Dr. William Green is here. I don't know whether he would like to call attention to the other complications or whether he thinks the observations are too inadequate to warrant mentioning.

DR. WILLIAM T. GREEN (by invitation), Boston: In March 1943 a child 5 years old was admitted with a severe type of active resistant rickets with marked deformities. It was decided to correct the deformities of the femurs and tibias during the active phase, since the bones, which showed marked decalcification, could be more readily fractured at this time; and we knew we could rapidly produce healing after correcting the deformities by the proper dosage of vitamin D. Under anesthesia the tibias were readily fractured manually and the femurs by an osteoclast. The corrected positions were maintained by a combination of traction and plaster splints.

The immediate postoperative course was uneventful, but on the eighth postoperative day this child, without preliminary warning, had a single, severe, prolonged convulsion which terminated coincidentally with the intravenous administration of calcium chloride. However, the patient did not have tetany; a calcium determination was performed on blood drawn during the convulsion. This child was unconscious for many days, and her mental recovery was extremely slow, although her reactions now are essentially normal.

We were forced to conclude by the process of elimination that fat embolism was the most likely explanation of this episode, although we were unable to prove its existence. Since fat embolism in children must be rare (we had never before recognized it as occurring and are not familiar with reports of its occurrence in persons of this age), the question arose as to whether the physical characteristics of bone during active rickets are such that they are conducive to fat embolism if surgical operations are performed during this phase. However, since that time we have had a similar experience with another child following osteotomy, and this child did not have rickets.

DR. PAUL GYÖRGY, Philadelphia: Biosynthesis of vitamins by the bacterial flora in the intestine might be of great importance with respect to the peculiar and spectacular difference between the intestinal flora of breast-fed and that of bottle-fed infants. The question arises whether the specific bifidus flora in breast-fed children is particularly suited to the human infant as a source of essential nutritional factors.

The second problem is the possibility of biosynthesis, not of vitamins alone but also of antibiotics, by the intestinal flora and specifically by *Lactobacillus bifidus* in breast-fed infants. During the past year I found, in collaboration with Dr. Worley at the Babies and Childrens Hospital, in Cleveland, some evidence that antibiotics are produced in infants and are excreted in the urine. The results were, however, erratic, and the study has to be expanded before the findings can be considered valid.

As a working hypothesis, one could perhaps assume that the natural immunity of the breast-fed infant is based, at least, in part, on biosynthesis of antibiotics by the intestinal flora.

DR. LASLO KAJDI, Baltimore: I wish to say that it is known that if a person is immobilized the serum calcium will rise. Therefore, in an effort to be cautious I followed at weekly intervals the levels of serum calcium and serum phosphorus, and the children clinically did not appear sick at the time of this high level of serum calcium. Although the blood chemistry showed this retrogression after the casts were removed, the roentgenograms which were taken showed continued healing of the rickets. I received a report from the mother about a year later, after the children went home, stating that they were doing very well.

Chemotherapy of Staphylococcus Aureus Infection of the Lung and Pleura in Infancy. DR. BENJAMIN KRAMER and DR. BENJAMIN PHILIPS (by invitation), Brooklyn.

Until recently the prognosis in severe suppurative disease of the lung and the pleural cavity in infancy due to *Staphylococcus aureus* has been grave. Kanof, Kramer and Carnes in 1939 (*J. Pediat.* **14**:712 [June] 1939) reported a mortality of 70 per cent in a series of 16 infants less than 1 year of age. In 1942, Clemens and Weems (*J. Pediat.* **20**:281 [March] 1942) reported on a series of 6 infants below the age of 2 years; all of these died despite chemotherapy. In summarizing the experience of Babies' Hospital from 1922 to 1943, Riley (*J. Pediat.* **24**:577 [May] 1944) reported a gross mortality of 34.5 per cent in 29 children up to 13 years and 55 per cent in 9 infants under 3 months of age. The greater severity of this illness in young infants was also noted by Hochberg and Kramer (*Am. J. Dis. Child.* **57**:1310 [June] 1939) and by Ladd and Swan (*New England J. Med.* **229**:1 [July 1] 1943). The latter observers reported a mortality of 66.7 per cent in 12 patients below the age of 4 months and 4.8 per cent in a series of 21 patients older than 4 months.

During the past year we have treated 5 infants less than 3 months of age who had suppurative disease of the lung and the pleural cavity due to *Staphylococcus aureus*; there were 4 recoveries and 1 fatality. The 1 fatality occurred in a moribund child, who died within eighteen hours after his admission to the hospital. This marked improvement in therapeutic results is attributable, we believe, to the use of penicillin. The following brief case histories give graphic proof of its great value. Incidental observations are reported concerning the course of the pulmonary and pleural lesions, the

indications for operation in empyema, the optimal dosage of the drug and possible reasons for the failure of therapy in the 1 fatal case. Although other children with infection due to *Staph. aureus* have been treated, this report is confined to very young infants because of the crucial nature of such a therapeutic test in this age group.

The 5 children in our series ranged in age from 4 to 12 weeks. All were critically ill on their admission to the hospital; they had extreme respiratory difficulty and cyanosis and showed clinical evidence of extensive pulmonary consolidation. Each of the 5 children received one of the sulfonamide compounds before his admission in a dose usually adequate for bronchopneumonia. In 4 instances this was ineffective. In 1 instance (patient II) the child appeared improved, but the empyema reappeared three days after the administration of sulfadiazine was discontinued. Penicillin therapy was instituted in each case only after the presence of *Staph. aureus* had been demonstrated by pleural aspiration. Of the 4 patients who recovered 2 received penicillin intrapleurally only (II and III) and 2 both intramuscularly and intrapleurally (I and IV). The total amount of penicillin administered to the patients who recovered was 70,000, 100,000, 450,000 and 640,000 Oxford units respectively, given over a period of seven to twenty-eight days. Thoracotomy and rib resection were necessary in 2 patients (III and IV)—in 1 (III) apparently because the empyema was loculated and penicillin had been repeatedly injected into one of the pockets, which was rendered sterile while the others were still positive. Supportive therapy, including administration of oxygen, parenteral administration of fluids and transfusions of blood, was given each child as indicated.

Only one difference is found when the course of treatment in our series is compared with that in previously reported series in an effort to explain our better therapeutic results. Obviously the additional agent was penicillin.

Final Session

Wednesday Morning, Sept. 27

The Crying of Newly Born Infants: The Community Phase. DR. C. ANDERSON ALDRICH, DR. CHIEH SUNG (by invitation), DR. CATHARINE KNOP (by invitation), GERALDINE STEVENS, R.N. (by invitation), and MARGARET BURRELL, B.Sc. (by invitation), Rochester, Minn.

This is the first of a series of reports on the crying of newly born babies. It comprises the results of thirty days' continuous observation of the amount of crying done by the infants in the nursery for the newborn at St. Mary's Hospital, Rochester, Minn. The data are analyzed in this report from the standpoint of the crying of the community of infants as distinguished from that of the individual babies.

Charts of the amount of crying as well as the amount of nursing care were made for each hour of every day. These were arranged so as to provide a diagram of the diurnal crying for the average baby per average day.

A reciprocal relationship between nursing care and amount of crying was clearly shown. It was also demonstrated that floor and nursing routines were reflected in the wailing of the babies. During this period the average baby cried nearly two hours daily.

It was possible to study statistically the number of babies crying at any one of seven hundred and twenty

instants. It was found that only 0.14 per cent of the time did as many as 50 per cent of the babies cry at once, while on the average about 10 per cent of them were vocalizing at any given instant. This makes it seem unlikely that crying in the nursery is largely contagious.

A slight but possibly significant correlation between crying and the barometric pressure was found.

Since crying in the neonatal period is a reflex, defensive mechanism, it would seem that a nursery routine which reduces the need for it should be the goal. From this preliminary survey it must be assumed that it will be necessary to increase nursery care in our present setup in order to improve the situation. In addition, the discrepancies which always crop up between nursery care and floor routines must be ironed out.

This report will be followed by a study, based on the same data, in which the crying of individual babies is considered.

DISCUSSION

DR. CHARLES HENDEE SMITH, New York: If there is one factor which Dr. Aldrich has not mentioned, it is the body warmth of these infants. I do not know how warm the babies are kept in his nursery, but if one walks past the nursery in any hospital, at least in my experience, one sees two thirds of the babies lying practically naked, wearing only a shirt and a diaper. They have kicked off the bedclothes and are lying with bare arms and legs. When they go home they are warmly wrapped up, because when the mother isn't bright enough to do it the grandmother is. She knows that a baby needs to be kept warm.

I wonder if that is not one of the factors which account for less crying at home than in the hospital. I have always felt that it was an outrageous thing for a mother to go into a private room in a hospital and pay up to \$36 or \$50 a day for it and have the baby put into a nursery where he is allowed to lie uncovered a great part of the time; it would never happen in a home. It is taking money under false pretenses, in my opinion, for a hospital to pretend to give adequate care to an infant and still expose him to chilling.

The temperature of the nursery is warm, no doubt, but if it is warm enough to keep the infant comfortable it is warm enough to make him sweat when he is covered, which isn't good for him. If it is not that warm, he will be chilled when he is uncovered. A person who goes to sleep without any bedding even in warm weather usually soon reaches for a sheet or a blanket to cover himself with. Moreover, warm nurseries make nurses perspire and tend to take cold when they go to a cooler room.

Some years ago in Montreal, Canada, I presented a simple device which I have used for nearly forty years, a little bag for babies. We used it in Bellevue for a great many years and it has been copied in many hospitals. I have used it for my private patients almost from the beginning. It consists merely of a light blanket folded over and sewed up across the shoulders. You might compare it to a split pillow case. The baby is put in it except for his head, and a couple of safety pins are put in the front so that he can't kick off his bedclothes. The mothers who use it are enthusiastic. It seems to be something that could be used to advantage in more hospitals and nurseries than is the case at present.

DR. C. ANDERSON ALDRICH, Rochester, Minn.: I have nothing to say in regard to Dr. Smith's remarks

except that we have an air-conditioned nursery in which the temperature is kept above 80 F. at all times. We did not attempt in this paper to go into the individual causes of crying, which will appear in a later report. I can say, however, that preconceived ideas about babies' crying mostly because they are hungry are inaccurate, because we are having a difficult time showing a significant correlation between the amount of crying and the amount of food that the babies get.

Self Feeding in Infancy. DR. CHARLES HENDEE SMITH, New York.

Most infants are well into the second year before they are considered by their mothers and by many students of child behavior to be capable of learning a practical technic of self feeding (Gesell says that self help is characteristic of the second year, beginning at 15 to 18 months. Bakwin says that at 12 to 14 months an infant may be taught to manage a spoon. Clara Davis says that a child may try to use a spoon at 6 months but may not be successful till 12 months or older. Bartlett says that a baby is usually fed most of his food to 2 or 2½ years.). No small number of children are still fed by the mothers until 4, 5 or even 6 years. The result is usually anorexia with all its attendant behavior problems. In the past five years a successful method of education in self feeding during the first year has been used with a large number of babies in private practice and in hospitals.

The first step is to make the baby hold his own bottle as soon as he is able to use his hands for voluntary grasping, at about 4½ months. A baby who holds his own bottle can easily be taught to hold his cup and to take orange juice from it at 4 to 5 months and milk at 7 to 8 months.

As soon as feeding of solid foods is begun—at 4½ to 5 months—the baby is taught to help with spoon feeding. (There is no special advantage in starting the feeding of solids earlier, and it is possible that too early feeding of solids underlies the antagonism to them shown by some babies.)

The technic of teaching spoon feeding is simple, but the mother must be shown exactly how to do it. She sits at the baby's right, facing in the same direction with her left arm behind him and supporting his back and her left hand holding his left arm and hand and keeping his hand out of the bowl of food. The baby's right hand is placed on the mother's little finger and if need be held there by her third finger. The spoon is held by her thumb and her index and middle fingers. Food is scooped into the spoon, which is then conveyed to the baby's mouth. After a few attempts, usually at the first lesson, he will pull on her finger toward his mouth. In a few days or weeks he will refuse food given in any other way, helping with every mouthful.

At 6 to 7 months the spoon is placed in the baby's hand and merely guided by the mother. He soon learns the scooping motion necessary to fill it. The spoon should be a teaspoon of standard size, bent so that his grasp of the curved end will keep the bowl horizontal as it approaches his mouth. The usual baby spoon is too small. A bib large enough to extend to the tray or table under the bowl saves the floor and the clothing so long as there is spilling. The mother may stand by with a "pick-up spoon" to take care of the food spilled.

By 8 months the baby can be taught to feed himself with some spilling and with very little help, mainly in scraping the dish. He will become adept long before 12 months. *Once started, this plan should never be*

abandoned; that is, no food should be given without having the infant share in the feeding.

This method of training makes it possible for the baby to feed himself many months before he would do so merely by observing the use of cup and spoon in the hands of others. Infants learn better by doing than by watching. If the mother makes an intelligent and patient effort there will be no failure. It is worth while to accelerate the baby's development in this mechanism because by this means he is removed at the earliest possible time from a state of parasitic dependency on his mother. Babies who have learned to feed themselves early rarely have behavior anorexia. Babies fed through the second year or later often have bad appetites. Although it takes a little more trouble to train the babies at first, it saves the mothers much time and anxiety later.

It may be concluded that babies should be able to feed themselves by 8 or 9 months and should not be fed by the mother into the second year.

DISCUSSION

DR. C. ANDERSON ALDRICH, Rochester, Minn.: I don't want to make this appear to be a duet this morning, but I think there is one aspect of Dr. Smith's remarks which is important to bring out, and which he just touched on. That is the fact that in conducting this education in self feeding of little babies, one is teaching them responsibility for their own existence, and it seems to me that that is one of the most important objects in rearing children—fostering a sense of responsibility for their own acts in such basic matters as eating, sleeping and eliminating. If one can get a baby from the beginning to take the responsibility for his own eating mechanisms, he is likely to take responsibility in other activities later.

DR. HUGH McCULLOCH, St. Louis: I think this is a duet of papers, decidedly. Their one strong note in common is that they are dealing with primitive, instinctive, essential activities of early life. One note that runs through both papers is the fact that most of our babies are burdened with artificial devices made by adults to control their activities. If they were left to their own activities they would behave much better.

Clinical Significance of Infants' Head Size. DR. JULIAN D. BOYD, Iowa City, Iowa.

This article will appear in full, with discussion, in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

The Effects of Marked Rickets in Early Childhood on Skeletal Development in Adolescence.

DR. ETHEL C. DUNHAM, Washington, D. C., and DR. HERBERT THOMS, (by invitation), New Haven, Conn. (From the Children's Bureau, United States Department of Labor, Washington, D. C., and the Department of Obstetrics and Gynecology, Yale University School of Medicine, New Haven, Conn.)

This report gives the case histories of 10 children who in early childhood had marked rickets, diagnosed from roentgenograms of the wrists. These children were included in the New Haven Rickets Study conducted by the Children's Bureau, United States Department of Labor, in the period 1923 to 1926 (Eliot, Martha M.: The Control of Rickets, *J. A. M. A.* **85**:656-661 [Aug. 29] 1925).

The children were reexamined in adolescence to determine the effect of the rachitic process on their skeletal development, especially that of the pelvis.

Physical examinations, certain anthropometric measurements, and roentgenograms of the pelvis of these 10 children were made when they were between 15 and 19 years old. Pelvic roentgenograms using two standard techniques were made and read by three obstetricians. The complete findings will form the basis of a separate report. The pelvic films were read by Dr. Thoms. The findings were as follows:

Nine of the 10 children who had had marked or moderate skeletal deformities still had some type of skeletal deformity in adolescence.

Eight of the 10 children had high sitting-height standing-height ratios, which were considered to be evidence of interference with growth of the extremities as well as of rachitic deformity.

Five of the 10 children were found in adolescence to have rachitic pelvis; 5 had normal pelvis. It was found that the older the child at the time that active rickets of moderate or marked degree was indicated by roentgenograms of the wrist, the greater was the incidence of rachitic pelvis in adolescence.

It was found also that in this small number of children knock knees were associated more often with rachitic pelvis than were bow legs.

The Use of 5 per Cent Sulfathiazole Ointment in an Emulsion Base for the Prevention and Treatment of Pyoderma in Newborn Infants.

DR. CHARLES A. WEYMULLER, Brooklyn.

At Long Island College Hospital 3,205 infants have so far been anointed just after birth with 15 Gm. of 5 per cent sulfathiazole ointment in a water-soluble base, in an attempt to prevent pustular infections. When the infants became exposed, they were reanointed with this preparation, the exposed nursery was closed and any infant with pyoderma was treated by evacuation of the pustules under 70 per cent alcohol, followed by frequent local application of 5 per cent sulfathiazole water-soluble ointment.

The experience has been excellent from August 1942 to August 1944 in that so far there have been only 4 sporadic cases of pyoderma, without spread to neighboring infants in the same nursery or to adjacent nurseries.

From 1930 to 1940, when pyoderma developed in an infant the child was isolated and treated by various current remedies. The nurseries were closed, and infants who acquired the disease were isolated. Of the 10,534 infants born at Long Island College Hospital during those ten years, 130 infants had pyoderma. The outbreaks were multiple and apparently self limited. There was much variation in severity.

Beginning in 1940 each newborn infant was anointed with 15 Gm. of 2 per cent ammoniated mercury ointment after being cleansed with sterile corn oil. When pyoderma supervened, all infants affected were isolated; the nursery was closed, and exposed infants were reanointed with 15 Gm. of 2 per cent ammoniated mercury ointment. From 1940 to 1942, 3,064 infants were so treated, and 35 had pyoderma. Outbreaks were multiple and varied. Ammoniated mercury ointment seldom limited spread or aided healing; dermatitis venenata was common, and the salve was difficult and disagreeable to handle. Since the introduction of 5 per cent sulfathiazole ointment in an emulsion base the results of treatment have been excellent, and the difficulties referred to are no longer encountered.

Laboratory studies of the 3,205 infants anointed with 5 per cent sulfathiazole ointment revealed the following data: The levels of blood sulfathiazole, the blood counts and the urine were not significantly altered. In 78 in-

stances the level of blood sulfathiazole (Jorgensen) varied between a trace and 1.6 mg. per hundred cubic centimeter—an average of 0.5 mg.

Forty-nine of the 3,205 infants who had had prophylactic inunction of 5 per cent sulfathiazole ointment in an emulsion base were readmitted for serious illnesses which required full doses of a sulfonamide compound. In 43 instances the drug employed was sulfathiazole. No instance of sensitization to sulfonamide compounds was encountered.

Admittedly, this short experience is insufficient to prove that this agent will always be so effective and that it will produce no disturbance. However, it has vastly improved the prevention and management of pustular infections of the newborn in the nurseries at Long Island College Hospital for these two years.

While most of these 3,205 infants apparently were protected by the application of sulfathiazole ointment immediately after birth, I do not wish to convey the impression that all pyodermas are due to infection acquired during the passage through the mother's birth canal. During the period covered by this study babies were discharged from the hospital between the seventh and tenth day after birth because of a shortage of maternity beds. Had they been kept in the hospital for two weeks, as was the former custom, more sporadic infections might possibly have occurred. Furthermore, the natural history of pyoderma in infants is characterized by periods of low incidence, even though no special control measures are taken. Several more years of observation, rather than larger numbers of cases, will show how well this new agent will hold up as an adjunct to good nursery technic.

The Influence of the Administration of Sulfanilamide on Acute Glomerulonephritis in Children.

DR. MILTON RAPOPORT (by invitation) and DR. MITCHELL I. RUBIN, Philadelphia.

The effect of the administration of sulfanilamide on the course of acute glomerulonephritis was evaluated in a group of 33 children with this disease. A comparable group of 40 children with acute glomerulonephritis not treated with sulfanilamide were used as controls. All children in both groups recovered completely from their disease, as most children with acute glomerulonephritis do, so that the comparison was concerned with the influence of sulfanilamide on the severity of the disease at its height and on the length of time required for complete healing. Sulfanilamide was administered in presumably adequate doses for five to eight weeks after the admission of each patient to the hospital.

The study indicated that the administration of sulfanilamide, despite its known ability to clear foci of infection due to beta hemolytic streptococci had no apparent effect on the renal lesion at its height, as measured by the time required for renal function, hypertension and cardiac abnormality to return to normal. Similarly there was no apparent effect on the length of time required for the renal lesion to heal completely, a combined normal routine urinalysis, a normal Addis sediment count and a normal sedimentation reaction being used as criteria of recovery. The value of sulfanilamide in controlling the infection antecedent to the nephritis is not negated, but it is felt that once nephritis is initiated in the child, this drug does not influence the "natural" course of the renal lesion.

DISCUSSION

DR. BENJAMIN KRAMER, Brooklyn: I should like to ask Dr. Rapoport what effect the therapy had on the

bacterial flora of the upper respiratory tract and whether foci of infection were removed as part of the therapy.

DR. MILTON J. RAPOPORT, Philadelphia: I cannot answer the question.

DR. WILLIAM L. BRADFORD, Rochester, N. Y.: I think one of the original claims was that sulfanilamide, when administered during the course of acute glomerulonephritis, helps to control exacerbations of a focal infection in the throat or in the sinuses.

I should like to inquire of Dr. Rapoport whether he has data concerning the occurrence of such flare-ups of infection in the two groups of patients. I should also like to ask about the presence of tonsils in the two groups.

DR. MILTON J. RAPOPORT, Philadelphia: In reply to Dr. Bradford's question, the infection preceding the flare-up of nephritis was detectable clinically, since the children were hospitalized continuously. Administration of sulfanilamide was apparently without influence on the number of flare-ups.

The difference in ultimate prognosis between our group of children and the patients in the Johns Hopkins study is impressive. It is widely appreciated that most children with acute glomerulonephritis go on to complete recovery: Our experience over a ten year period has been a rate of recovery of almost 98 per cent, complete recovery usually taking place within six months of the time of onset. In the Johns Hopkins group a large percentage (up to 50 per cent) became chronic nephritic patients. Apparently the natural course of acute glomerulonephritis is different in the adult, chronic nephritis developing in a large percentage, whereas the child almost always recovers completely.

DR. HENRY F. HELMHOLZ, Rochester, Minn.: There are two points that I should like to raise. The first regards the cause of nephritis. Is it a sensitization? Practically nothing is known about the causation of nephritis. I think it is gradually being accepted that rheumatic fever is related in some way to hemolytic streptococci, and this relationship has been demonstrated probably better than in any other way by the effect of giving sulfanilamide as a prophylactic.

Does this same relationship hold with regard to nephritis? I think possibly the best explanation of the causation of nephritis is that it is a sensitization produced somehow in the renal tissue to a foreign protein, possibly some product of hemolytic streptococci. The fact that there has been no such relationship between therapy with sulfonamide compounds and recurrences, as has been shown by Longcope, is of significance.

I should like to emphasize, however, the fact that the prevention of the disease rather than its cure is the outstanding principle in the treatment of rheumatic fever, and I think it is of importance to follow up this work experimentally as a possible means of a further attack on nephritis, for in this field physicians are certainly starting from scratch.

DR. ALLAN M. BUTLER, Boston: Is it fair to say that the vascular disturbances that occur in children with nephritis are greater than such manifestations in older patients, and that in older patients there is a high incidence of the phenomena due to sensitivity? If so, it might be suggested that in older patients there is more of the sensitivity aspect similar to the sensitivity to streptococcal infection in rheumatic fever, whereas in younger patients the symptomatology of the disease and the possibility of permanent damage to the kidneys

are more closely related to acute vascular disturbance and less closely to the phenomena of sensitivity.

If all that should be true (and I realize that it may not be), it would account for the difference in the emphasis which the pediatrician as contrasted with the internist places on the magnesium sulfate therapy which specifically lessens the vascular spasm and the resulting disturbances.

DR. MILTON J. RAPOPORT, Philadelphia: I agree entirely with Dr. Butler. In the Johns Hopkins study, the antistreptolysin titer remained elevated for about the same length of time in the control group and in the group treated with sulfanilamide. Why this titer should have persisted at a high level for as long as six months after the patient's discharge from the hospital is not clear: Apparently sulfanilamide therapy had no effect on the antistreptolysin titer.

DR. MITCHELL I. RUBIN, Philadelphia: The one important point of difference between the patients studied by the Baltimore group and our patients is age. The natural course of the disease in the two groups is different, the rate of recovery of the young children being about 95 per cent, whereas that of the adults was closer to 60 per cent. Thus any benefits from therapy with sulfonamide compounds would be less apparent in the younger age group. Nevertheless, there is no evidence even of shortening of the disease process in our group. In both groups cardiac involvement, as demonstrated by the electrocardiogram, was high. I know of 2 young adults in whom death resulted from heart failure.

DR. ALLAN M. BUTLER, Boston: May I ask, how about the manifestations of cerebral injury which might result?

DR. MITCHELL I. RUBIN, Philadelphia: In answer to your question, Dr. Butler, regarding cerebral manifestation in adults, of a group of about 15 young adults 2 had marked cerebral symptoms. Thus it would appear that the nature of the disease in the child and in the adult must be similar, a fact which makes it difficult at this time to assess the factors which vary the prognosis for the two groups.

Summary of a Three Year Study of the Clinical Application of Disinfection of Air by Glycol Vapors. DR. JOSEPH STOKES JR., and DR. T. N. HARRIS (by invitation), Philadelphia.

The clinical application of disinfection of air by glycol vapors has been investigated for three winters at the Children's Seashore House in Atlantic City. These studies involved primarily the determination of the rate of incidence of infections of the respiratory tract in groups of patients whose supply of air was largely disinfected and in control groups.

This institution, a convalescent home, was selected because the prevailing conditions were peculiarly well adapted to the exhibition of the clinical effects of air disinfection.

Propylene and triethylene glycol were used. The degree of disinfection of air was determined by settling plate counts of bacterial colonies; the concentration of glycol vapors was determined by chemical procedures.

It was found that whereas 132 infections of the respiratory tract occurred in eighty-one weeks in the control wards, 13 such infections occurred at the same time in comparable control wards. An epidemic of common colds during one winter showed an even better ratio, of 79 such infections to 3. Counts of bacterial colonies were reduced by propylene glycol vapor from

81 to 13 per Petri plate per hour, and the concentration of propylene glycol vapor in the air was maintained in the neighborhood of 0.069 mg. per liter.

It is concluded that the chemical disinfection of air can be applied to the clinical problem of the control of air-borne cross infection with satisfactory results under similarly favorable conditions.

DR. CULVER: May I ask a question? Was there much evidence of any toxic effect of these vapors on the persons exposed to them?

DR. T. N. HARRIS, Philadelphia: No, there is no evidence of that at all. We should not rest on our observations made in the course of the experiment itself. Extensive studies have been made on various animals by Dr. Robertson of Chicago, in which he used an order of magnitude much higher than anything to which children could be exposed.

DR. ALLAN M. BUTLER, Boston: Over what periods of time?

DR. T. N. HARRIS, Philadelphia: That study has been running for well over a year, probably over eighteen months.

DR. ALLAN M. BUTLER, Boston: And the animals were continuously exposed to such vapors?

DR. T. N. HARRIS, Philadelphia: Yes, and other animals had it by oral administration. There were pathologic studies in those experiments.

DR. S. GRAHAM ROSS, Montreal: Dr. Harris, is one sensible of the presence of this substance?

DR. T. N. HARRIS, Philadelphia: Well, I am, but most people are not. I can detect a faint sweetish quality in the air after I have been breathing air containing a concentration completely adequate for disinfecting purposes, but I do not think I ever met anyone else who was so sensible of it.

DR. S. GRAHAM ROSS, Montreal: You may be sensitized to it.

DR. T. N. HARRIS, Philadelphia: I do not think so; I could notice the vapor at the very beginning of our experiments.

Attempts to Find Poliomyelitis Virus in Fish.

DR. JOHN A. TOOMEY, Cleveland.

Using Kramer's technic, stool contents were prepared from fish, and the virus was looked for.

Though the virus was possibly found once, I did not know where it had come from—the fish or the handlers. Even though it might have come from the fish, it was not felt that this fact was of great epidemiologic significance, because fish are gutted before sale and simple cooking destroys the virus. The handlers of these fish in the epidemic area may well have been carriers.

I then attempted to immunize carp in various ways. Although I allowed the fish to feed on the virus and likewise injected it, I failed absolutely to demonstrate the presence of the virus in the gastrointestinal contents or the presence of neutralizing antibodies in the blood serum of the fish, even though I waited for over a year after immunizing the fish to collect the latter specimens. This result is unusual, for in every other species used neutralizing antibodies can be easily demonstrated.

Metabolic Studies in Hereditary Periodic Paralysis. DR. IRVINE MCQUARRIE and DR. M. R. ZIEGLER (by invitation), Minneapolis.

Eight of 13 siblings in the family reported on are known to suffer from periodic episodes of flaccid paralysis. These children represent the third generation which has exhibited this tendency as a dominant heredi-

tary trait. One of the children, a 17 year old youth died in a paralytic attack when the respiratory muscle became involved. A second boy, aged 15 years, served as a subject for the present studies. It was found that attacks of paralysis could be induced at will by administering 150 Gm. of dextrose by mouth or by injecting 50 units of insulin. In such induced attacks, as well as in spontaneous episodes of paralysis, both the potassium and the inorganic phosphorus of the serum were reduced to subnormal levels. Potassium chloride given by mouth in 1 Gm. doses every hour interfered with the induction of paralytic attacks by dextrose and inulin, even when hypoglycemic reactions occurred. In one experiment sodium phosphate given similarly prevented the induction of an attack by administration of dextrose. However, this salt, unlike potassium chloride was ineffective in relieving paralytic attacks which had already developed.

Institution of a seventy-two hour fast at a time when the patient was having severe attacks every day on an ordinary mixed diet resulted in a rise of the serum potassium to normal and in freedom from paralysis. No attacks occurred as long as he was maintained on a milk diet, but when sufficient carbohydrate was added to raise the ratio of dextrose to potassium above 75 they recurred. A high protein, low carbohydrate diet (protein 170 Gm., carbohydrate 5 Gm. and fat 80 Gm.) allowed freedom from attacks even when the potassium intake was low (0.5 Gm. daily), while a high fat, low carbohydrate diet (fat 260 Gm., carbohydrate 10 Gm. and protein 84 Gm.) was unfavorable (potassium 0.60 to 1 Gm.). The ratio of preformed carbohydrate to potassium in the diet which was the threshold for attacks varied with the type of diet, being between 70 and 80 with the high protein, low carbohydrate diet or milk diet and approximately 10 with the high fat, low carbohydrate diet. The ratio decreased as the amount of preformed carbohydrate was increased.

DISCUSSION

DR. BENJAMIN KRAMER, Brooklyn: I wonder whether Dr. McQuarrie correlated the various effects of changes in diet and the intensity of the attacks with the potassium in the blood. As a rule, I think the attacks come on when the level of potassium is about 10 mg or less per hundred cubic centimeters.

DR. IRVINE MCQUARRIE, Minneapolis: Yes. Serum potassium values were determined at fairly frequent intervals throughout the entire period of study. All attacks of paralysis were associated with reduced values usually below 12 mg. per hundred cubic centimeters. During periods of freedom from attacks, normal levels were usually found. When the carbohydrate to potassium ratio of the diet approached the threshold for attacks, serum values fluctuated between 12 and 15 mg per hundred cubic centimeters.

DR. BENJAMIN KRAMER, Brooklyn: Well, does it matter how the potassium fluctuates in the diet?

DR. IRVINE MCQUARRIE, Minneapolis: Our results indicate that wide fluctuations in the potassium content of the diet may be made without the occurrence of paralytic attacks so long as the carbohydrate to potassium ratio falls below certain levels. The last vary somewhat with the proportions of protein, carbohydrate and fat in the diet.

Pseudodoxia Pediatrica. DR. HARRY BAKWIN, New York.

The subject of this essay is the persistence in pediatrics of theories and practices even though their falsity is patent or has been demonstrated.

Advances in medicine are made not only by the discovery of new principles, information and technics but by the discarding of false teachings and practices as well. Among the erroneous practices only recently abandoned are cleansing the mouths of infants after feeding, use of oil drops in the nose, vigorous removal of the vernix caseosa, early operation for empyema and osteomyelitis and overrigid feeding schedules.

That indiscriminate tonsillectomy is beneficial to children is a false idea which has persisted for many years. A survey conducted in New York city ten years ago by the American Child Health Association showed that over 60 per cent of children 11 years of age in some of the public schools had had their tonsils removed. It was found that when the children whose tonsils had not been removed were reexamined 3 times by groups of physicians, only 65 of 1,000 children had not had tonsillectomy recommended.

Myringotomy is also practiced too freely on children. It was possible to reduce the incidence of running ears at Bellevue Hospital in infants under 2 years to a little more than a third of its previous rate by limiting otoscopic examinations and by laying down stringent criteria for myringotomy. The use of mastoidectomy for infants was correspondingly reduced.

There is no reason to believe that the indiscriminate delivery of babies in hospitals is beneficial to either mothers or babies. The increase in the proportion of deliveries in hospitals bears no demonstrable relation to either maternal or neonatal mortality or morbidity. The results obtained by the Frontier Nursing Service in Kentucky, where over 97 per cent of deliveries are done in the home by midwives, are striking. The maternal mortality for the first 4,000 deliveries was less than one seventh of that for the white population of the United States as a whole.

Hospitals are unsuited for the care of the newborn. Separation of mother and baby at this early age is unphysiologic and without precedent in the mammalian world. The rigid rules in the hospital make breast feeding difficult. Infections in babies are not infrequent and account for considerable mortality.

Older infants, too, suffer in hospitals because of the isolation generally considered necessary in order to limit cross infections. Infants need the stimulation which comes from contact with other human beings.

The indiscriminate use of vitamin supplements for children is without adequate basis. Eating has been endowed with a moralistic aura; it should, instead, be

a pleasure. Eating is an integral part of the culture of the home and the family.

Other erroneous practices are the unnecessary treatment of physiologic bowing of the legs, the premature use of orthodontia, the diagnosis and treatment of rickets on insufficient evidence, the use of unnecessarily expensive sugars and the use of vitamin D during the summer months.

A major error in medical education is failure to train students properly for practice in the home. The student is not taught the indications for laboratory aids in the home. He soon learns that he is not able to obtain the tests which he believes are necessary and consequently feels that he is doing slipshod work. This gives him a feeling of inadequacy and interferes with the sense of satisfaction in his work to which he is entitled. A further error in medical education is failure to impress the student with the significance of disease and death to the family group.

DR. CHARLES HENDEE SMITH, New York: I should like to reinforce Dr. Bakwin's statement that too extensive laboratory work is demanded by most students. In the course of my teaching I regularly asked my students what were the essentials that they would demand in making a diagnosis in a simple case of pneumonia or any other febrile disease; I then put what they asked on the board and added up the cost. They wanted about \$150 worth of work on every febrile case before they would venture a diagnosis.

Another thing about which I should like to add a word is the too early feeding of solids to young infants. I think that is one of the greatest errors which have crept into modern practice. Many of you who are not practicing may not know it, but the average physician in pediatric private practice begins to feed solids at 6 weeks or less. Babies do just as well if solids are given only at 4½ to 5 months.

Dr. Bakwin's remarks about vitamin D are worthy of reinforcement. I have taken a number of babies of intelligent mothers within the last few years and withheld from them all vitamin D in the form of added cod liver oil, etc. I have made the mother expose the child's face or other parts of his body to the sun in summer and winter, and there has been no evidence of rickets in this group of children. In the climate of middle New Jersey, where there is pretty good sunshine all winter, they get along just about as well as children who have had cod liver oil.

Book Reviews

Fractures and Dislocations for Practitioners. Third edition. By Edwin O. Geckeler, M.D. Price, \$4.50. Pp. 361, with 320 illustrations. Baltimore: The Williams & Wilkins Company, 1943.

This book, a third edition, includes two parts, (1) fractures and (2) dislocations, and an index, all within 361 pages. In successive chapters appear discussions of general considerations, including definition and process of bony repair and its failures, roentgen examination, medicolegal aspects of fractures, complications and hospital organization. Then follow in order chapters on emergency treatment, fracture wounds, reduction, immobilization and follow-up treatment. Individual chapters on the various parts of the skeleton complete the first part of the book. The second part describes some dislocations, including those of the temporomandibular joint, spinal and sacroiliac joints and joints of the clavicle, shoulder, elbow, wrist, hand, hip, knee, ankle and foot, in varying degrees of elaboration. The chapter on facial bones and jaws seems weak, and the chapter on the vertebrae leaves the reader with confused ideas as there is too much repetition and reference to isolated cases. Much information is packed into this volume, and the plentiful illustrations are reasonably illuminating. The author cultivates a curt and often too positive style (some of the statements may be doubted) and sometimes leaves much to be desired in the structure of sentences. In medical writing brief expressions may be simultaneously pleasing and informative. Some editing is needed; the pain associated with fractures of the sacrum is described as "moderate"; "linear tenderness" is mentioned, and the term "drunken cases" is used as on page 99. Several methods are referred to as the Jahss method of treatment of fracture of the pelvis, but no description is given. In treatment of fracture of the body of the scapula, the practitioner is told to apply a Velpeau dressing with the shoulder held back. The reviewer believes this to be an impossible act. On page 140 the hanging cast is described as "an extra heavy circular plaster dressing," extending from the axilla to the knuckles; Caldwell repeatedly warned that it should not be "extra heavy." There are other too broad and apparently thoughtless statements, for example "failure to replace the epiphysis (femur at knee, which is not always displaced in one direction as stated) will result in retarded growth of the limb." There are few typographic errors in the text, and the book is well bound and of agreeable size. For the practitioner who knows considerable about fractures this volume may offer a quick reference to assist him in his daily problems; it can hardly be recommended to the medical student as a basic guide.

Body Poise. By Walter Truslow, M.D., F.A.C.S. Price, \$4.50. Pp. 312, with 96 illustrations. Baltimore: Williams and Wilkins Company, 1943.

Dr. Truslow, who is a consulting orthopedic surgeon for a number of hospitals in the city of New York, has written this book primarily for those who are interested in posture, or, as it is more recently designated, body mechanics. These would include orthopedic surgeons,

pediatricians with an interest in posture and laymen interested in physical training and body development. It is written in the style typical of textbooks.

In the first part of the book the author deals with the anatomy of the human body, especially as it applies to the structures involved in the maintenance of a good figure. In turn, a good figure, Dr. Truslow states, is conducive to good general health and improved functioning of the various organs of the body. In this part of the book he also analyzes the gymnastic kinesiology of the motor mechanism of the human frame. He describes eight fundamental positions from which corrective exercises can be started.

Since feet are important in maintaining good posture, a chapter in the second part of the book is devoted to the anatomy and kinesiology of the foot. He describes methods for examining and measuring the arches and for recording their height-length index. He also discusses the treatment of weak feet by both active and passive methods.

Several chapters are devoted to an analysis of faulty posture. Dr. Truslow classifies variations in the antero-posterior plane of the body, as the gorilla type and the kangaroo type. He also discusses faulty posture due to lateral curvature of the spine. He describes and explains the use of the spinometer, an instrument for measuring the variations in the spinal curvature. Two types of exercises are described for the improvement of faulty posture: (1) muscle-developing and (2) posture-training exercises.

The last chapters in the volume are concerned with the kinesiology of various sports. The author's descriptions of sports, and his analysis of the various necessary movements are interesting and detailed. In general, the sports that require bilateral, symmetric movements are the most beneficial.

There is a good glossary of anatomic terms at the end of the book, and there are ample and descriptive illustrations.

Young Offenders. By A. M. Carr-Saunders, Hermann Mannheim and E. C. Rhodes. Price, \$1.75. Pp. 168, with no illustrations. New York: The Macmillan Company, 1944.

An investigation of juvenile delinquency was carried out in London and six smaller towns by means of studies of nearly 2,000 delinquent and an equal number of nondelinquent children. The delinquent children were boys who were brought into court beginning Oct. 1, 1938. Sixty social and economic factors were considered for each child including such items as attitude of the parents, income of the family, school record, interests, social activities, working habits and gang affiliations of the boy.

The results indicate that broken homes, abnormal home atmospheres (over-laxity or overstrictness), over-crowding of homes, poor conduct in school and the laxity of parents in allowing adolescent children out at night contribute to delinquency. The author theorizes concerning the "lower immunity" of some children to environmental conditions that lead to delinquency. "We never discover that all delinquents have been subject to one kind of influence or show some distinctive characteristic."

This is entirely a statistical study. The onset of the war prevented the prosecution of psychologic studies which were planned. As the author concludes this study like all similar ones gives little information on the exact reasons why individual children become delinquent. The report is well written and represents a great deal of work and study.

Textbook of General Surgery. By Warren H. Cole, M.D., and Robert Elman, M.D. Fourth Edition. Price, \$10. Pp. 1,170, with 955 illustrations. New York: D. Appleton-Century Company, Inc., 1944.

This book is a well organized presentation of general surgery. Practically all of the illustrations are original and represent material the authors have seen at the University of Illinois and Washington University. Many of the small technical details of surgical procedure that confront an intern or resident are well described. There is a complete chapter on surgical intervention in relation to diabetes with illustrations of the more common diabetic lesions.

The authors mention the tannic acid method first among the ways of treatment of burns. There has been so much criticism of this method that I believe its dangers and limitations should also have been presented. Some of the chapters contain detailed outlines which are of value for rapid review and as a summary of the subject. Included in the book is a chapter on war surgery which briefly presents this broad field.

In conclusion, this is a sound textbook of general surgery which is clearly written in a simple understandable style and which will be of greatest value to the student, intern and resident surgeon. It is a book that the teacher would find easy to use because of the excellent organization of material.

Radiation and Climatic Therapy of Chronic Pulmonary Diseases. By Edgar Mayer, F.A.C.P., F.A.C.C.P. Price, \$5.00. Pp. 393, with illustrations. Baltimore: Williams & Wilkins Company, 1944.

The editor, Dr. Mayer, and twenty-two collaborators participated in writing this book. It is divided into five sections, which deal successively with (1) the physics, physiologic action and sources of light; (2) the artificial light therapy of different clinical forms of tuberculosis; (3) the effects of climate, weather, altitude and solar radiation on tuberculosis and other pulmonary diseases; (4) the roentgen treatment of intrathoracic tumors and of tuberculosis of different organs and parts of the body, and (5) the surgical versus the conservative therapy of tuberculosis of bones and joints.

The book presents a thorough and conservative evaluation of the indications, contraindications, limitations, beneficial effects and possible harmful effects of radiation and climatic therapy. This evaluation of climate and radiation as adjuvants to other therapeutic measures represents deductions based on the wide clinical experience of the various authors and on their familiarity with the literature. The book contains more than five hundred references to pertinent literature.

Guiding the Normal Child. By Agatha H. Bowley, Ph.D. Price, \$3.00. Pp. 174, without illustrations. New York: Philosophical Library, Inc., 1943.

The author states that "the purpose of this book is to give a brief account of the normal growth and development of children from babyhood to adolescence, to indicate when and how difficulties occur and to show how they can be best handled. The book is

written primarily for the student who is training to be a teacher, but it is also suitable for parents."

The author carries out her purpose well considering that the whole subject of growth and development from infancy through adolescence, intellectual as well as emotional, normal and abnormal, is covered in one hundred and forty pages. With only nine pages devoted to adolescence, for example, only a brief, superficial consideration of the subject is possible. Since the author is a teacher and the director of a child guidance clinic (in England), she devotes more time to children of school age than to those of the other age groups. The Freudian viewpoint is followed in explaining problems.

There is a good but brief final chapter on children and the war. The book is well written and interesting.

Family Nutrition. By Rachel M. Winlock, M.D.; Emerson R. Sausser, D.D.S.; Joseph Stokes Jr. M.D.; James J. Waygood, M.D.; Anna de Planter Bowes, M.A., and Pauline Beery Mack, Ph.D. Second edition. Price, 50 cents. Pp. 119, with 22 tables. Philadelphia: The Philadelphia Child Health Society, 1943.

The first edition of "Family Nutrition" was published in April 1942 and reviewed in the *AMERICAN JOURNAL OF DISEASES OF CHILDREN* (64:762, 1942). The chief differences in the second edition are the inclusion of a chapter on "Menu Planning and Rationing," additional data in the chapter on the "Measuring of Nutritional Status" and a discussion of the more recently recognized members of the vitamin B complex in the chapter on "The Nutritional Needs of People."

La eosinofilia masiva de origen infeccioso y evolucion regresiva, como una nueva entidad clinica. By Teodosio Valledor. Paper. Price, not given. Pp. 52, with 17 illustrations. Habana, Cuba: Molina y Compania, 1944.

This monograph written in Spanish is a more complete account (6 observations on children and 3 on adults) of a new symptom complex first reported by the author in 1939. The condition consists of fever, catarrh and adenopathy with 30,000 to 70,000 white cells, of which 80 per cent are eosinophils. There is also a granulation of lung tissue, which is shown in illustrative roentgenograms. The bone marrow shows a hyperplasia of eosinophilic forms, as do the lymph nodes. The disease has a tendency to recovery in two years. No good etiologic factor was found.

Allergy in Practice. By Samuel Feinberg, M.D. Price, \$8. Pp. 777, with 36 illustrations. Chicago: Year Book Publishing Co., 1944.

Of the 777 pages in this book 392 are devoted to the general principles of allergy and to the exciting agents of allergy, such as pollens, molds, foods and injected substances, and their modes of operation; the rest of the book deals with the diagnosis and treatment of various allergic disorders.

There are not many illustrations. This, however, does not detract from the value of the book. The meat is in the text, and the meat is good. In books on allergy, in which many references must be made to the original work of other men, it often happens that so many references are made that there is little of the author to be found in the book. Dr. Feinberg has avoided this. He has expressed in clear, judicial and

easily read language what he himself has seen and thinks and what the general opinion of allergists is. Discussions of controversial subjects and descriptions of methods the value of which is not proved are printed in small type, and by this means the author has clearly separated the generally accepted from the debatable. He is not extreme in any way; his opinions are sane and his conclusions just. The majority of allergists would agree with them.

The book is practical, and still the author has not neglected the fundamental and often theoretic concepts on which a proper understanding of allergy depends. The sections on allergic responses to drugs and pollens are particularly good, and that on allergy to molds (64 pages) based on the author's well known original work, is the most complete to be found anywhere.

There are minor points here and there throughout the book with which some allergists would disagree, and inasmuch as allergy in childhood is so common and so important, the book would be improved if a special section were devoted to this subject. There is little concerning allergy in childhood in it except a few pages on infantile eczema. This, however, is a minor criticism, and any pediatrician interested in allergy should own the book. It is the most readable book on allergy with which the reviewer is familiar. It is not superficial, nor on the other hand is it superscientific. In short, it is a thoroughly sane, adequate, well presented exposition of a difficult subject by an obviously intelligent well balanced man. The reviewer recommends it unreservedly.

Contribución al estudio humoral en las deshidrataciones agudas del lactante. By Eugenio A. Ruiz. Price not given. Pp. 53, with tables. Santiago, Chile: El Chileno, 1943.

This is a thesis issued by the Eugenio Ruiz Memorial Commission of the University of Chile. It includes discussions of the index of refraction, the protein content and the volume and quantity of red cells in the blood of 33 children under 1 year of age with dehydration. Tables of the results are given. The most noteworthy deviation from the normal was the increase in the content of protein in the blood. In 5 instances in which the level of protein was reduced, edema was present.

Finger Prints, Palms and Soles: an Introduction to Dermatoglyphics. By Dr. Harold Cummins and Dr. Charles Midlo. Price, \$4.00. Pp. 281, with 144 illustrations. Philadelphia: The Blakiston Company, 1943.

This book is a scholarly and authoritative study in dermatoglyphics. Dr. Cummins is professor of microscopic anatomy, and Dr. Midlo is associate professor in the same department at Tulane University School of Medicine. The first part of the book deals with the history of the study and the details of making and interpreting prints. The last part has to do with the biologic significance of such studies. Of particular interest to pediatricians is the chapter on the diagnosis of twins.

El sueño normal y patológico en el niño. By Bernard Vijnovsky. Price not given. Paper. Pp. 342. Buenos Aires: El Ateneo, 1944.

This book written in Spanish deals with sleep in children. The first part describes the mechanism and

physiology of the normal sleep reflex; then pathologic variations. These include all forms of epilepsy, narcolepsy, pikenolepsy and such disorders. They are all illustrated by clinical observations taken from the author's clinic. There is also an excellent bibliography of 212 articles. The subject matter is well organized, and the viewpoint taken is interesting.

Enfermedad quística del pulmón en la infancia. By Teodosia Valledor. Paper. Price, not given. Pp. 132, with 75 illustrations. Editorial Neptuno. Cuba: Habana, 1944.

This monograph written in Spanish deals with 17 cases of cystic disease of the lung observed by the author, who is professor of pediatrics at the University of Habana, over a period of ten years. He believes that the condition is a congenital malformation due to mesodermic hyperplasia in which the affected zones remain in the fetal stage of development. The prognosis is unfavorable and in small children grave. The only satisfactory treatment is surgical removal of the areas (lobectomy or pneumectomy).

Rorschach's Test. Volume I. By Samuel J. Beck, Ph.D. Price, \$3.50. Pp. 223, with 20 tables and 10 figures. New York: Grune & Stratton, 1944.

Of the large number of tests which have been devised for and used in attempts to determine characteristics of personality, the Rorschach test is one of the few that are still used. The subject is shown a series of 10 ink blots and asked to state everything that comes to his mind from looking at them. The test material is devised to stimulate free association with fixed stimuli having no specific meaning.

This volume records in detail the types of responses that have been secured by the author during over twenty years' experience. He has set up general norms by comparison with which an examiner can recognize unusual or abnormal responses.

The book does not include a description of the ink blots themselves; the reader is referred to earlier publications for this. The material is prepared for the psychologist who uses the test rather than for the lay reader who may be interested in the general information which a test of this sort can give. A great deal of time has evidently been used in preparing the volume, and one can assume that it is authoritative.

Hospital Discharge Study: Volume II: Hospitalized Illness in New York City. By Neva R. Deardorff, Ph.D., and Marta Fraenkel, M.D. Price \$1.00 (all three volumes, \$2.00). Pp. 349 with no illustrations. New York: Welfare Council of New York City, 1943.

This second volume is devoted to the medical aspects of discharges from hospitals in New York city. As a statistical study of the records of over 500,000 patients discharged from these hospitals in a single year, it contains much information of value to public health departments, social agencies, health and hospital insurance agencies, hospital administrators and socially minded physicians.

Advances in Internal Medicine, Volume I. Edited by J. Murray Steele, M.D. Price, \$4.50. Pp. 292 with 19 illustrations and 8 tables. New York: Interscience Publishers, Inc., 1942.

As stated in the preface this series of volumes is offered to provide, under the sponsorship of an out-

standing editorial board, a summary of those fields in which progress has occurred recently.

This volume contains summaries of: the use of the Miller-Abbot tube in the diagnosis and treatment of disorders of the gastrointestinal tract; the use of insulin and protamice zinc insulin in the treatment of diabetes; the sympathetic control of the peripheral vascular system; the antibacterial action of the sulfonamide drugs; the choice of the sulfonamide drugs in the treatment of infection; infections of the urinary tract; present trends in the study of epidemic influenza; the pathogenesis and treatment of hypertension, and nephrosis and riboflavin deficiency. Each summary includes a bibliography.

This volume fills a real need, and the continued publication of the series will be a contribution to the library of every physician.

Principles and Practices of Inhalational Therapy.

By Alvin L. Barach, M.D. Price, \$4.00. Pp. 315, with 59 illustrations. Philadelphia: J. B. Lippincott Company, 1944.

This is a comprehensive and authoritative book on the physiologic basis and technics of inhalational therapy. The author is particularly well qualified to write such a book by virtue of his extensive clinical and experimental training in this field. The text is concise, carefully edited and practical in content and presentation. It is an excellent summary and a careful evaluation of the entire field. The material covers the historical and physiologic background of inhalational therapy in all its aspects from the use of gases, positive pressure and respirators and the equalizing of chest pressure to the use of vaporized solutions with sympathomimetic drugs. The author summarizes the etiology, pathologic physiology, symptoms and management by inhalational therapy of acute anoxia (acute altitude sickness), pulmonary diseases, cardiac and cardiovascular diseases, migraine, seasickness, hemorrhage and many other conditions for which inhalational therapy is of value. Besides the material on the use of inhalational therapy for over 30 clinical conditions of general medical interest, there is a discussion of asphyxia of the newborn which should be of special interest to the pediatrician and the obstetrician. The book will have a special appeal to physicians engaged in military medicine, and the sections on injuries of the lungs caused by blasts, aerial transportation of patients with miscellaneous diseases, poisoning by oxygen and war gases, submarine medicine and caisson disease are of specialized interest. The chapter on research aspects of therapy by means of the respiratory functions is both instructive and provocative and summarizes the present and future state of the therapeutic use of gases in clinical medicine. There are five excellent and practical chapters devoted to methods and technics for using apparatus intended for the administration of the various types of gas. This discussion covers tents, catheters, masks, respirators and incubators. The last chapter is devoted to the determination of the concentration of oxygen and of carbon dioxide in inspired air in masks and in other equipment used in therapy by means of oxygen.

The book not only is one of the most comprehensive and yet concise collections of critically evaluated current data on inhalational therapy but serves as a practical guide to persons charged with operating equipment used

in this type of treatment. The text is well documented, with a selected and up-to-date bibliography and 59 clear and explicit illustrations. The book deserves a place in the library of every practicing physician and will be especially useful to nurses and technicians to provide a rational background for the use of inhalational equipment. Anesthetists and students of anesthesiology will find this an authoritative contribution in their field.

Handbook of Nutrition. By Many Contributors.

Price, \$2.50. Pp. 586. Chicago: American Medical Association, 1943.

The "Handbook of Nutrition" is a symposium on nutrition written for physicians and for all others who are interested in the field of nutrition. Each article is contributed by an authority in his particular field. The keynote of the book is the role of nutrition in the advance of the human race. The purpose of the book is to amplify the knowledge of nutrition. Stiebeling says in her chapter on American diets: "As far as the immediate or long term well-being of a person can be improved through dietary betterment, that person falls short of being truly well fed."

The first chapters deal with constituents of food—proteins, fats, minerals and vitamins; calories; the human requirement; the role of the various nutritional elements in metabolism, and their incorporation into the daily food intake.

There follows a discussion of the changes in the composition of foods, especially in their vitamin and mineral content, which may be brought about by processing—that is, by storage, freezing, canning and dehydrating. The need for limiting the reductions in food value that take place as a result of processing is clearly demonstrated.

Next, consideration is given to the improvement of the common foods (for example, the enrichment of flour) for the purpose of providing the essentials of nutrition more adequately to every one. Some factors in the problem of providing adequate nutrition to all are income level, size of family and home management.

The last chapters are devoted to present day methods of appraisal of the state of nutrition, deficiency diseases and their prevention and the use of diet in the treatment of disease.

This book presents a complete nutritional study and is one which every physician and every other person interested in nutrition will wish to own.

News and Comment

PERSONAL NEWS

New Appointments for Dr. L. Emmett Holt Jr. and Dr. James L. Wilson.—Dr. L. Emmett Holt Jr., associate professor of pediatrics at Johns Hopkins Medical School, has been appointed professor of pediatrics at the New York University College of Medicine and director of pediatrics service at Bellevue Hospital.

Dr. James L. Wilson, who previously held this position, has accepted the chair of pediatrics at the University of Michigan.

Directory of Pediatric Societies *

INTERNATIONAL

INTERNATIONAL ASSOCIATION OF PREVENTIVE PEDIATRICS

President: Prof. S. Monrad, Dronning Louises Børne-hospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

INTERNATIONAL CONGRESS OF PEDIATRICS

President: Dr. Henry F. Helmholtz, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Charles F. McKhann, University Hospital, Ann Arbor, Mich.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston. Time: Postponed indefinitely.

INTERNATIONAL CONGRESS FOR THE PROTECTION OF INFANCY

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

ARGENTINE PEDIATRIC SOCIETY OF BUENOS AIRES

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Largaia, Cerrito 1179, Buenos Aires.

ASSOCIAÇÃO PAULISTA DE MEDICINA, SECTION ON PEDIATRICS

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Paulo de Barros Franca, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.

BRITISH PAEDIATRIC ASSOCIATION

President: Prof. L. G. Parsons, 58 Calthorpe Rd., Five Ways, Birmingham.
Secretary: Dr. Donald Paterson, 27 Devonshire Pl., London, W. 1.

DANISH PEDIATRIC SOCIETY

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børne-hospital, Copenhagen.

NEDERLANDISCHE VEREENIGING VOOR KINDER-GENEESKUNDE

President: Dr. J. H. G. Carstens, Servaasbolwerk 14a, Utrecht.
Secretary: Dr. R. P. van de Kastele, Laan van Poot 340, 's Gravenhage.
Place: Different places. Time: Three times a year.

PAEDIATRICKÝ SPOLOK NA SLOVENSKU

President: Dr. A. J. C. Churá, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Dr. E. A. Ccckayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosenbaum, 26 Bialkstr., Tel Aviv.
Secretary: Dr. A. Brünz, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Angel A. Aballí Arellano, 17 No. 609 Vedado, Habana.
Secretary: Dr. Julio G. Cabrera Calderin, Hospital Mercedes L y 21 (Vedado), Box 2430, Habana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Fernando López Clares, 12/a. Medellín 191, Mexico.
Secretary: Dr. Jesus Gómez Pagola, Versalles 64, Mexico.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. E. Santcs Mendoza.
Secretary: Dr. P. Oropeza, Hospital de Niños, Caracas.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weil-Hallé, 49 Avenue Raymond Poincare, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Jose Alberto Praderi, Eduardo Acevedo 1132, Montevideo.
Secretary: Dr. Alfredo Ramon Guerra, Paysandú 824, Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.
Place: Philadelphia. Time: June 18-22, 1945.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Franklin P. Gengenbach, 1850 Gilpin St., Denver, Colo.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S
HOSPITAL SECTION

Chairman: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly, Mass.

AMERICAN PEDIATRIC SOCIETY

President: Dr. James L. Gamble, 300 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES
OF CHILDREN

President: Dr. R. R. Struthers, 906 Drummond Medical Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Edward M. Bridge, 219 Bryant St., Buffalo, N. Y.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia 46.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Eugene Smith, 385-24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Warren R. Sisson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. C. G. Ashley, 833 S. W. 11th Ave., Portland, Ore.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. Arild E. Hansen, University of Minnesota, Minneapolis.
Secretary-Treasurer: Dr. Albert V. Stoesser, 205 W. University Hospital, Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester.
Time: January, April, July and October.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver.

SOUTHERN MEDICAL ASSOCIATION, SECTION
OF PEDIATRICS

Chairman: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.
Secretary: Dr. Angus McBryde, 604 W. Chapel Hill St., Durham, N. C.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Amas Gipson, 948 Forrest Ave., Gadsden.
Secretary-Treasurer: Dr. Ruth Berrey, 2021-6th Ave. N., Birmingham.

ARIZONA PEDIATRIC SOCIETY

President: Dr. Vivian Tappan, San Clemente, Tucson.
Secretary: Dr. Hilda Kroeger, Arizona State Health Dept. (Maternal and Child Welfare Division), Phoenix.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION
ON PEDIATRICS

Chairman: Dr. William C. Deamer, University of California Hospital, San Francisco.
Secretary: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Ludo Von Meysenbug, Box 3356, Daytona Beach.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. T. F. Davenport, 104 Ponce de Leon Ave. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB
OF CONNECTICUT

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Time: Three meetings a year.

ILLINOIS STATE MEDICAL SOCIETY, SECTION
ON PEDIATRICS

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Mark L. Floyd, Children's Hospital, Iowa City.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION
ON PEDIATRICS

Chairman: Dr. A. Clement Silverman, 608 E. Genesee St., Syracuse.
Secretary: Dr. Albert G. Davis, 307 Gas and Electric Bldg., Utica.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA,
PEDIATRIC SECTION

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

MICHIGAN STATE MEDICAL SOCIETY,
PEDIATRIC SECTION

Chairman: Dr. Charles F. McKhann, University Hospital, Ann Arbor.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. E. W. Hancock, 820 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. John M. Thomas, 1102 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Arthur H. London, 1105 W. Main St., Durham.
Secretary: Dr. Jay M. Arena, 604 W. Chapel Hill St., Durham.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Ben H. Nicholson, 301 N. W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Lonita Boggs, 301 E. Coffee St., Greenville.
Secretary-Treasurer: Dr. Hilla Sheriff, Wade Hampton Office Bldg., Columbia.

TEXAS PEDIATRIC SOCIETY

President: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Secretary-Treasurer: Dr. John E. Ashby, 3510 Fairmount Ave., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Edwin A. Harper, 301 Rivermont Ave., Lynchburg.
Secretary: Dr. Emily Gardner, 1100 W. Franklin St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY,
SECTION ON PEDIATRICS

President: Dr. Andrew Amick, 1021 Quarrier St., Charleston.
Secretary: Dr. A. A. Shawkey, Professional Bldg., Charleston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND
PEDIATRIC SECTION

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. I. B. Silber, 10465 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO,
SECTION OF PEDIATRICS

President: Dr. I. Nelles Silverthorne, 170 St. George St., Toronto, Canada.
Secretary: Dr. G. P. Hamblin, 2333 Bloor St. W., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry J. Cohen, 1975 Walton Ave., New York.
Secretary: Dr. Walter Levy, 12 E. 88th St., New York.
Place: Concourse Plaza Hotel, 161st St., and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Harry A. Naumer, 37-8th Ave., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Granada Hotel. Time: Fourth Wednesday of October, November, February, March and April.

BUFFALO PEDIATRIC SOCIETY

President: Dr. A. Wilmot Jacobsen, 187 Bryant St., Buffalo N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Edward J. Wynkoop, 501 James St., Syracuse.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Morley D. McNeal, 2 N. Sheridan Rd., Highland Park, Ill.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

CINCINNATI PEDIATRIC SOCIETY

Secretary: Dr. T. Selkirk, 3530 Reading Rd., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati.
Time: On call.
President: Dr. Lloyd K. Felter, 3144 Jefferson Ave., Cincinnati.

DALLAS PEDIATRIC SOCIETY

President: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas, Texas.
Secretary-Treasurer: Dr. Gladys J. Fashena, 4585 Bel-
fort, Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second
and fourth Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. John J. Pollack, 650 Maccabees Bldg.,
Detroit, Mich.
Secretary: Dr. Philip J. Howard, 2799 W. Grand Blvd.,
Detroit, Mich.
Place: Wayne County Medical Society. Time: 8:30
p. m., first Wednesday of each month from October
to June, inclusive.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRICS
SECTION (ATLANTA, GA.)

Chairman: Dr. Don F. Cathcart, 478 Peachtree St.
N. E., Atlanta.
Secretary: Dr. Harry Lange, 478 Peachtree St., N. E.,
Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E.
Time: Second Thursday of each month from October
to April, 8 p. m.

HOUSTON PEDIATRIC SOCIETY

President: Dr. Raymond Cohen, 2300 Caroline St.,
Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd.,
Houston, Texas.
Place: College Inn, Houston. Time: Fourth Monday
of each month.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Edwin H. Schorer, 1103 Grand Ave.,
Kansas City.
Secretary: Dr. H. E. Petersen, Kirkpatrick Bldg., St.
Joseph, Mo.
Place: Kansas City General Hospital. Time: On call.

LOS ANGELES COUNTY MEDICAL ASSOCIATION,
PEDIATRIC SECTION

President: Dr. Oscar Reiss, 2200 W. 3d St., Los
Angeles.
Secretary-Treasurer: Dr. Elena Boder, 1830½ Lucille
Ave., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925
Wilshire Blvd. Time: Second Monday of February,
April, June, October and December.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND
THE ACADEMY OF MEDICINE OF BROOKLYN,
PEDIATRIC SECTION

President: Dr. Abraham M. Litvak, 1145 Eastern Park-
way, Brooklyn.
Secretary: Dr. Harold Levy, 750 St. Marks Ave.,
Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m.,
fourth Monday of each month, October to April,
inclusive.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC.,
SECTION ON PEDIATRICS

Chairman: Dr. Meyercon Coe, 217-02-91st Ave., Queens
Village, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th
Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills,
N. Y. Time: Third Monday of October, January,
March and May.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA,
SECTION ON PEDIATRICS

President: Dr. Harry A. Spigel, 2647 Connecticut Ave.,
Washington, D. C.
Secretary-Treasurer: Dr. Perry W. Gard, 2520 Wood-
ley Rd., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time:
8 p. m., fourth Thursday of every month.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. F. T. Mitchell, 376 S. Bellevue Ave.,
Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madi-
son Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. B. J. Malnekoff, 3213 N. Marietta Ave.,
Milwaukee.
Secretary-Treasurer: Dr. R. M. Hall, 324 E. Wisconsin
Ave., Milwaukee.
Place: Milwaukee Athletic Club. Time: Second Wednes-
day of each alternate month, beginning with February.

NEW YORK ACADEMY OF MEDICINE, SECTION
OF PEDIATRICS

Chairman: Dr. Howard Craig, 175 E. 79th St., New
York.
Secretary: Dr. Alfred E. Fischer, 73 E. 90th St., New
York.
Place: New York Academy of Medicine, 2 E. 103d St.
Time: Second Thursday of each month from October
to May, inclusive, 8:30 p. m.

NORTHERN CALIFORNIA AFFILIATES

President: Dr. Crawford Bost, 400 Post St., San
Francisco.
Secretary: Dr. William A. Reilly, 384 Post St., San
Francisco.
Time: Second Thursday of September, November,
January, March and May.

OKLAHOMA CITY PEDIATRIC SOCIETY

President: Dr. William M. Taylor, 1200 N. Walker
St., Oklahoma City.
Secretary: Dr. G. R. Felts, 625 N. W. 10th St., Okla-
homa City.
Place: Oklahoma Club. Time: Third Thursday of
each month.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Carl Fischer, Greene and Coulter Sts.,
Germantown, Philadelphia.
Secretary: Dr. Sherman Little, 1740 Bainbridge St.,
Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time:
Second Tuesday in January, March, May and
November.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown, Pa.

Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh.

Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Stanley Meade, 913 Floyd Ave., Richmond, Va.

Secretary-Treasurer: Dr. Louise Galvin, 214 S. Boulevard, Richmond, Va.

Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Herbert Soule, 122 Rutgers St., Rochester, N. Y.

Secretary-Treasurer: Dr. Jerome Glaser, 300 S. Goodman St., Rochester, N. Y.

Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Jerome Diamond, 508 N. Grand Ave., St. Louis.

Secretary-Treasurer: Dr. Mary A. McLoon, 408 Humboldt Bldg., St. Louis.

Place: St. Louis Medical Society Bldg. Time: First Friday of each month from November to June.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Frederick B. Joy, Stimson Bldg., Seattle.
Secretary: Dr. Sherod M. Billington, Medical Dental Bldg., Seattle.

Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.

Secretary: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.

Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Campbell Harvey, 35 W. Huron St., Pontiac, Mich.

Secretary: Dr. Harry A. Towsley, University of Michigan, Department of Pediatrics and Communicable Diseases, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRICS SECTION (NEW YORK)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.

Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.

Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.

SALICYLATE INTOXICATION

STUDIES ON THE EFFECTS OF SODIUM SALICYLATE ON PROTHROMBIN TIME AND ALKALI RESERVE

GLADYS J. FASHENA, M.D., AND JAMES N. WALKER, M.D.

DALLAS, TEXAS

Salicylate therapy has been in use for over half a century for the treatment of acute rheumatic fever, and opinions have varied among clinicians as to the mode of action and the value of the salicyl compounds. Although most authorities have agreed that these drugs exert definite antipyretic and analgesic actions, few have maintained that salicylates actually modify the course of the disease. Tremendous interest has been aroused, therefore, by Coburn's recent report¹ that massive doses of sodium salicylate produce a prompt subsidence of rheumatic inflammation if a level of blood salicyl (measured as salicylic acid) above 350 micrograms per cubic centimeter is maintained. To maintain such a level, Coburn advocated the daily administration of from 10 to 20 Gm. of the drug. This amount exceeds the toxic and even the fatal dose as given in some textbooks of pharmacology.²

Numerous reports of salicylate poisoning in children have appeared in the literature,³ which indicates that the salicyl compounds are not always the harmless household remedy that they are generally thought to be. In view of the probability of greatly increased use of this group of drugs in the treatment of rheumatic fever and the observation that rheumatic patients metabolize salicylic acid in a different manner

from normal persons,⁴ it seems pertinent to report a case of salicylate poisoning occurring during the treatment by the Coburn method of a patient with acute rheumatic fever.

REPORT OF A CASE

V. R. G., a 9 year old Negro boy, was admitted to the hospital on May 23, 1944, with pain in the lower parts of the legs and calves for four days as the chief complaint.

History.—The family history was noncontributory. The patient's history was also irrelevant except for the fact that he had had several bouts of mild fever associated with pharyngitis during the preceding winter. These attacks had lasted for one or two days and had been associated with pain in the lower parts of the legs but with no pain in the joints. Tonsillectomy had been performed in 1937. An injury to the left eyeball with hemorrhage into the anterior chamber had been sustained in May 1943.

The present illness began with mild pharyngitis and fever four days before the patient's admission to the hospital. At the same time aching pain in the calves and the lower parts of the legs was noted. The pain in the calves persisted and became slightly worse each day. The patient vomited once on the day before admission and had one large, watery, green stool without pus or blood on that day.

Physical Examination.—Physical examination at the time of his entry into the hospital revealed a well developed and nourished Negro boy, who did not appear acutely ill. His temperature was 102 F. His pulse rate was 88 per minute and his respiratory rate 22. There was an opacity of the left cornea 2 mm. in diameter; the left pupil was elliptic in its vertical axis and did not respond to light or in accommodation. The ears, nose and throat were not unusual except for a few tags of lymphoid hyperemic tissue in the tonsillar fossae. The neck was supple, the expansion and the external appearance of the chest were within normal limits and the lungs were entirely clear to percussion and auscultation. The heart was not enlarged to percussion, and the point of maximal apical impulse was felt in the fifth interspace 1.5 cm. within the midclavicular line. Regular sinus rhythm was present, the heart sounds were of good quality and no murmurs were heard. The abdomen was soft and flat, and the tip of the spleen was felt 1 cm. below the costal margin on deep inspiration. There was

4. Hanzlik, P. J.; Scott, R. W., and Thoburn, T. W.: The Salicylates: V. Excretion of Salicyl in the Urines of Rheumatic and Non-Rheumatic Individuals, *J. Pharmacol. & Exper. Therap.* **9**:247-267 (Feb.) 1917.

From the Departments of Pathology and Pediatrics, Southwestern Medical College, and the Children's Medical Center.

1. Coburn, A. F.: Salicylate Therapy in Rheumatic Fever: A Rational Technique, *Bull. Johns Hopkins Hosp.* **73**:435-464 (Dec.) 1943.

2. Goodman, L., and Gilman, A.: *The Pharmacological Basis of Therapeutics*, New York, The Macmillan Company, 1941. Sollmann, T.: *A Manual of Pharmacology*, ed. 5, Philadelphia, W. B. Saunders Company, 1936.

3. Barnett, H. L.; Powers, J. R.; Benward, J. H., and Hartmann, A. F.: Salicylate Intoxication in Infants and Children, *J. Pediat.* **21**:214-223 (Aug.) 1942. Stevenson, C. S.: Oil of Wintergreen Poisoning: Report of Three Cases, One with Autopsy, and a Review of the Literature, *Am. J. M. Sc.* **193**:772-788 (June) 1937.

slight tenderness to pressure over the medial malleolus of the right ankle, but no swelling or redness was visible. The results of the neurologic examination were within normal limits.

Laboratory Data.—Laboratory studies on admission to the hospital were as follows: The urine showed no protein, sugar or abnormally formed elements. Analysis of the blood showed a hemoglobin content of 3.9 Gm. per hundred cubic centimeters, a red cell count of 4,500,000 and a white cell count of 23,250, with 64 per cent adult polymorphonuclear leukocytes, 22 per cent immature forms, 11 per cent lymphocytes, 1 per cent monocytes and 3 per cent eosinophils. A test for sickling gave negative results. The erythrocyte sedimentation rate (Westergren) was 90 mm. in one hour. Wassermann and Eagle complement fixation tests gave negative results. Microscopic examination of the stool showed

the PR interval to 0.26 second and showed minor changes in the ST segment.

A diagnosis of acute rheumatic fever was made, and oral sodium salicylate therapy, 6 Gm. per day, was started. The fever did not decrease appreciably in response to the administration of sodium salicylate, but the pain and swelling in the joints decreased rapidly. In four days all evidence of involvement of the joints had disappeared. Administration of the drug was stopped at this time, with almost immediate appearance of pain in both shoulders and in the joint of the right elbow.

Four days later administration of sodium salicylate, in oral doses of 8 Gm. per day, was resumed, with prompt disappearance of the symptoms in the joints. On this day the heart was found by physical and fluoroscopic examinations to be moderately enlarged. After forty-eight hours of drug therapy at this higher level the patient began to breathe more rapidly and more

Summary of Clinical and Hematologic Observations in a Case of Acute Salicylate Poisoning (V. R. G.)

Date	Daily Medication	Bleeding Time	Clotting Time	Pro-thrombin Time	Respiratory Rate	Comment
5/26	S.S.* 6 Gm.	20-25	
5/27	S.S. 6 Gm.	20-25	
5/28	S.S. 6 Gm.	20-25	
5/29	S.S. 6 Gm.	20-25	
5/30	None	20-25	
5/31	None	20-25	
6/ 1	None	20-25	
6/ 2	S.S. 5.3 Gm.	20-25	
6/ 3	S.S. 8 Gm.	25-30	
6/ 4	S.S. 8 Gm.	36-40	Kussmaul breathing noted
6/ 5	S.S. 8 Gm.	36-44	More severe hyperpnea and vomiting
6/ 6	S.S. 8 Gm.	38-44	Severe hyperpnea, vomiting and hallucinations
6/ 7	S.S. 8 Gm.	44-46	Severe hyperpnea, vomiting and hallucinations
6/ 8	S.S. stopped; syn. vit. K 1 mg./4	5'30"	10'	2'45"	44-46	Blood carbon dioxide content 33 vol. %; urine acid, but no ketones present; albuminuria 2+, white cells and casts present
6/ 9	None	2'30"	4'	75"	28-35	Hyperpnea less marked but still present
6/10	None	1'30"	2'	45"	20-25	Respirations normal
6/11-13	No medication given and no unusual symptoms noted
6/14	A.S.A.† 0.6 Gm.	20-25	No symptoms
6/15	A.S.A. 1 Gm.	25"	20-25	No symptoms
6/16	A.S.A. 1 Gm.	57"	20-25	No symptoms; no blood salicyl detected
6/17	A.S.A. 1 Gm.	20-25	No symptoms
6/18	A.S.A. 1 Gm.	20-25	No symptoms
6/19	A.S.A. 1 Gm.	17"	20-25	No symptoms; no blood salicyl detected
6/20	A.S.A. 1.6 Gm.	1'45"	2'	70"	20-25	No symptoms; no blood salicyl detected
6/21	A.S.A. 1.6 Gm.	3'	4'	1'55"	20-25	
6/22	A.S.A. 1.6 Gm.	2'30"	3'30"	1'25"	20-25	No symptoms; syn. vit. K started, 1 mg. i.m. daily
6/23	A.S.A. 1.6 Gm.	1'30"	2'	45"	20-25	Blood salicyl, 57.6 micrograms per cubic centimeter
6/24	A.S.A. 2 Gm.	50"	20-25	Blood salicyl, 81.6 micrograms per cubic centimeter
6/25-27	A.S.A. 2 Gm.	
6/28	A.S.A. 2 Gm.	30"	20-25	No symptoms
6/29-30	A.S.A. 2 Gm.	
7/ 1	A.S.A. 2 Gm.	40"	20-25	No symptoms
7/ 2-4	A.S.A. 2 Gm.	
7/ 5	A.S.A. 2 Gm.	25"	Blood salicyl, 86 micrograms per cubic centimeter

* Sodium salicylate.

† Acetylsalicylic acid.

a few red cells, but no other abnormalities. A spinal tap revealed normal fluid under normal pressure. The patient's serum did not agglutinate typhoid A or H, paratyphoid A or B, Proteus OX 19 or Brucella abortus antigens in any dilution. The streptococcus antifibrinolysin test gave a 1 plus reaction.

Therapy and Clinical Course.—The patient's temperature fluctuated between 101 and 104 F. for the first eight days. It was thought that he might have typhoid, but repeated cultures of the blood and of the stool failed to reveal *Bacillus typhosus*. Two days after his admission, pain, swelling and tenderness appeared in both knee joints, and on the following day fluid was present in both joints. Pain in the fingers and wrists made its appearance on the following day. The pulse, which had been relatively slow in relation to the temperature, began to increase in rate, and on the patient's fourth day in the hospital the average rate was 110. An electrocardiographic tracing at this time revealed a prolongation of

deeply than usual. On the following day the hyperpnea became more striking; it resembled Kussmaul breathing except that it was slightly more rapid. On each succeeding day the hyperpnea became more severe. Nausea and vomiting appeared on the third day of therapy at the higher level, and disorientation and hallucinations supervened on the sixth day. At this time the heart rate averaged 110 per minute, and a gallop rhythm was present. The lungs were free of rales, and there was no enlargement or tenderness of the liver or edema. The venous pressure was 110 mm. of water, and the circulation time (dechoin sodium) was eighteen seconds.

On the seventh day the patient appeared gravely ill. The hyperpnea showed no response to oxygen or to change from the recumbent to the sitting posture. The patient was semicomatose and disoriented, and it was the impression of several examiners that the symptoms were of central rather than of cardiac or pulmonary origin. Examination of the blood showed a bleeding

time of five minutes and thirty seconds, a clotting time of ten minutes and a prothrombin time of two minutes and forty-five seconds, a value more than five times the normal, which connotes almost complete absence of circulating prothrombin. The carbon dioxide-combining power was 33 volumes per cent. The urinary p_H was 5. No ketones were present in the urine, but the Gerhardt test gave a deep purple color characteristic of salicylates. Albumin was present in the urine, and many white cells and finely granular casts were found in it.

Salicylate therapy was stopped, and synthetic vitamin K (synkamin [5,4-amino-2-methyl-1-naphthol]) was administered parenterally in 1 mg. doses four times during the day. As may be seen in the table, recovery from the hypoprothrombinemia and the hyperpnea was rapid. In forty-eight hours the patient's respirations were normal and the sensorium clear. The bleeding, clotting and prothrombin times approached normal values, and the urine became normal. The patient's subsequent course was interesting in that relatively small doses of acetylsalicylic acid produced prothrombinopenia, which regressed briefly on one occasion without the administration of vitamin K even though salicylate therapy was maintained. Prolongation of the prothrombin time was noted on two occasions when the amount of circulating salicyl was so small as to escape detection by chemical test. Synthetic vitamin K in daily parenteral doses of 1 mg. only partially controlled the hypoprothrombinemia.

PROBLEMS IN SALICYLATE INTOXICATION

That salicylate intoxication can produce many of the symptoms exhibited by this patient is well recognized, but there seems to be no general agreement concerning the mechanism underlying the various physiologic disturbances. On the basis of experiments with animals, the hyperpnea has been attributed by Johnson⁵ to a fixed acid acidosis resulting from accumulation of lactic acid and other fixed acids. Odin,⁶ Barnett, Powers, Benward and Hartman³ and Dodd, Minot and Arena,⁷ on the other hand, have demonstrated that hyperpnea may supervene when the blood and the urinary p_H are normal or above normal, a fact which suggests primary hyperventilation. The first two studies cited expressed the view that the salicyl radical directly stimulates the respiratory center; the work of Dodd and her associates with animals led these authors to the conclusion that changes in body temperature, the sensation of heat and the increase in gaseous exchange induced by salicylates are more important factors than central stimulation.

Hypoprothrombinemia induced by salicylates was first demonstrated by Link, Overman, Sul-

livan, Huebner and Scheel,⁸ whose studies on dicoumarin (3,3'-methylenebis [4-hydroxycoumarin]), the active agent producing hemorrhagic sweet clover disease in animals, suggested that this compound may break down into salicylic acid in the body. These authors were able to produce prothrombinopenia by feeding salicylates to rats deficient in vitamin K, and many of the animals so treated died with hemorrhagic manifestations similar to those seen in sweet clover disease. Recent studies have shown that similar effects may occur in human beings even when there is no evidence of previous vitamin K deficiency. Meyer and Howard⁹ have reported that vitamin K will protect completely against the reduction in prothrombin if it is given in conjunction with salicylates. Shapiro¹⁰ estimated that approximately 1 mg. of synthetic vitamin K will counteract the prothrombin-reducing action of 1 Gm. of acetylsalicylic acid, even if it is given after the drop in prothrombin has occurred. Rapoport and his associates,¹¹ during investigations on the effects of large doses of salicylates on the electrolyte structure of the blood, noted that many rabbits intoxicated with salicylate died of pericardial hemorrhage during heart puncture. These authors then studied 15 rheumatic patients during periods of salicylate medication and found significant prolongations of the prothrombin time in 8 of them.

Many questions arise in connection with the observed side effects of the salicylates. The mechanism by which hypoprothrombinemia is produced is obscure. No quantitative observations have been made correlating the blood salicyl level with the change in prothrombin. No unanimity of opinion exists as to whether sodium salicylate induces acidosis in the human subject. Ketosis has been observed many times in cases of salicylate poisoning, but whether this condition represents a direct response to the drug or merely a starvation effect is unknown. In an attempt

8. Link, K. P.; Overman, R. S.; Sullivan, W. R.; Huebner, C. F., and Scheel, L. D.: Studies on the Hemorrhagic Sweet Clover Disease: XI. Hypoprothrombinemia in the Rat Induced by Salicylic Acid, *J. Biol. Chem.* **147**:463-474 (Feb.) 1943.

9. Meyer, O. O., and Howard, B.: Production of Hypoprothrombinemia and Hypocoagulability of the Blood with Salicylates, *Proc. Soc. Exper. Biol. & Med.* **53**:234-237 (June) 1943.

10. Shapiro, S.: Studies on Prothrombin: VI. The Effect of Synthetic Vitamin K on the Prothrombinopenia Induced by Salicylate in Man, *J. A. M. A.* **125**:546-548 (June 24) 1944.

11. Rapoport, S.; Wing, M., and Guest, G. M.: Hypoprothrombinemia After Salicylate Administration in Man and Rabbits, *Proc. Soc. Exper. Biol. & Med.* **63**:40-41 (May) 1943.

5. Johnson, C. C.: The Salicylates: The Question of Acidosis Following Administration of Salicylates, *J. A. M. A.* **94**:784-789 (March 15) 1930.

6. Odin, M.: Is Salicylate Poisoning an Acidosis? *Acta med. Scand.*, 1932, supp. 50, pp. 177-186.

7. Dodd, K.; Minot, A. S., and Arena, J. M.: Salicylate Poisoning: An Explanation of the More Serious Manifestations, *Am. J. Dis. Child.* **53**:1435-1446 (June) 1937.

to throw some light on these problems, the following studies were undertaken.

EXPERIMENTAL STUDIES

Subjects.—Six hospitalized children ranging in age from 6 to 11 years were chosen for the study. There were 4 boys and 2 girls. Five of the 6 were convalescent from orthopedic disorders and were entirely well except for their healing local lesions. The sixth (J. E.) had chorea and acute rheumatic carditis. All had eaten a general ward diet for at least ten days before the start of the experimental period. No medicines were administered for a week preceding the observations.

Procedure.—Control determinations of blood salicyl level, alkali reserve, bleeding, clotting and prothrombin times, urinary p_H and the other urinary constituents recorded in the accompanying charts were made for all subjects during the first twenty-four hour period.

bath and analyzed for carbon dioxide-combining power within thirty minutes. Salicyl levels were determined later the same day. Daily urinalyses were carried out promptly on the first voided specimen of the day.

The blood salicyl was determined by the method of Brodie, Udenfriend and Coburn,¹² in which the level of salicylic acid in the blood is taken as the measure of blood salicyl. The carbon dioxide-combining power of the blood was determined by the Van Slyke manometric technic. The bleeding time was estimated by a standardized needle prick of the left index finger. The clotting time was measured on capillary blood by the capillary tube method. The prothrombin time was determined by the Quick method,¹³ using desiccated rabbit brain thromboplastin which had been stored in vacuo.¹⁴ The normal prothrombin time by this method ranged from twenty to twenty-eight seconds, with an average value of twenty-five seconds. The urinary p_H was determined with nitrazine paper. The standard Benedict

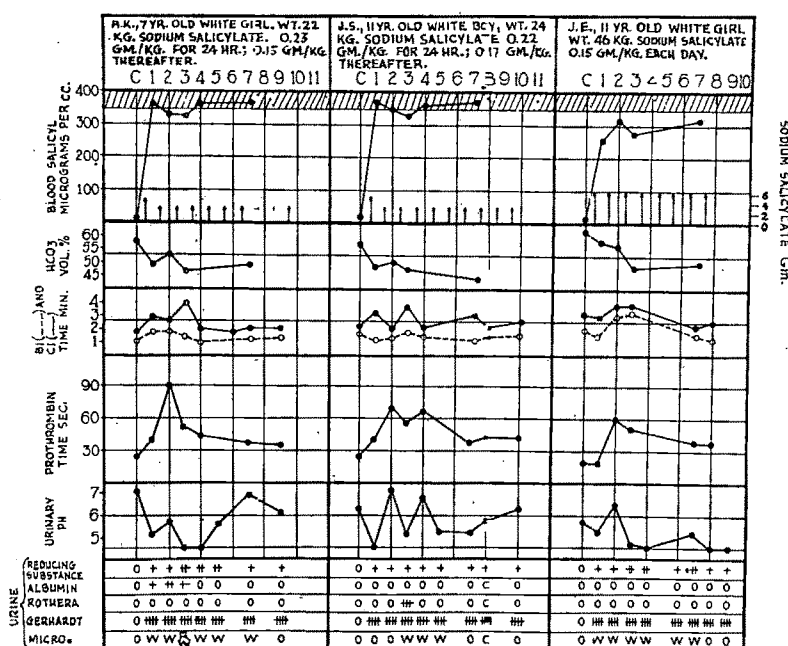


Chart 1.—Effects of administering sodium salicylate to 3 patients at levels of from 0.23 Gm. to 0.15 Gm. per kilogram of body weight per twenty-four hours on the blood salicyl level, alkali reserve, bleeding, clotting and prothrombin time, urinary p_H and other chemical and microscopic constituents of urine. The arrows designate the total amount of sodium salicylate ingested each day. The control values are designated by C. The shaded area in the blood salicyl column represents the "therapeutic level" deemed necessary by Coburn (see text). The designations W and R in the column for microscopic examination of urine refer to white blood cells and red blood cells respectively.

Sodium salicylate was subsequently administered by mouth at four hour intervals in the following amounts: (1) 0.22 Gm. per kilogram per twenty-four hours, (2) 0.15 Gm. per kilogram per twenty-four hours and (3) 0.09 Gm. per kilogram per twenty-four hours. In the 2 children who received 0.22 Gm. per kilogram nausea, vomiting and tinnitus developed after twenty-four hours of therapy, necessitating a drop to 0.17 and 0.15 Gm. per kilogram respectively; this dosage was maintained for the remainder of the experimental period. Medication was continued from four to seven days. Blood for chemical analysis was drawn under oil from the fasting subjects each morning, placed immediately in an anise

qualitative test was used to detect urinary reducing substance; all other tests on urine were carried out according to standard procedures.

12. Brodie, B. B.; Udenfriend, S., and Coburn, A. F.: The Determination of Salicylic Acid in Plasma, *J. Pharmacol. & Exper. Therap.* **80**:114-117 (Jan.) 1944.

13. Quick, A. J.: *The Hemorrhagic Diseases and the Physiology of Hemostasis*, Springfield, Ill., Charles C Thomas, Publisher, 1942.

14. The thromboplastin used in this study was supplied by the Department of Medical Research, Winthrop Chemical Co.

RESULTS

Charts 1 and 2 show the results obtained.

Blood Salicyl Level.—It is noteworthy that only the subjects who received 0.2 and 0.22 Gm. per kilogram for the first twenty-four hours attained blood salicyl levels which Coburn would consider adequate for the treatment of rheumatic fever. In both of these children toxic symptoms (tinnitus and vomiting) developed within twenty-four hours; so the dose was reduced to 0.15 and 0.17 Gm. respectively, with complete disappearance of toxic effects. In spite of this reduction in dosage, levels over 350 micrograms (of salicylic acid) per cubic centimeter of blood were maintained. The subjects who received only the latter dose of the drug throughout the experi-

pnea or hyperpnea. There was no consistent rise in the p_H of the urine, and acetonuria was not demonstrated except in sporadic instances. In view of the lack of respiratory change and the persistence of acid urine, accumulation of fixed acid offers the most likely explanation for the fall in alkali reserve.

Clotting Mechanism.—In every instance the prothrombin time showed marked prolongation, the first change occurring within twenty-four hours of the start of administration of the drug. By the second day the hypoprothrombinemia was at its height, but thereafter there was a spontaneous drop in prothrombin time in spite of continued salicylate therapy. In no instance were the normal pretreatment levels reached, but

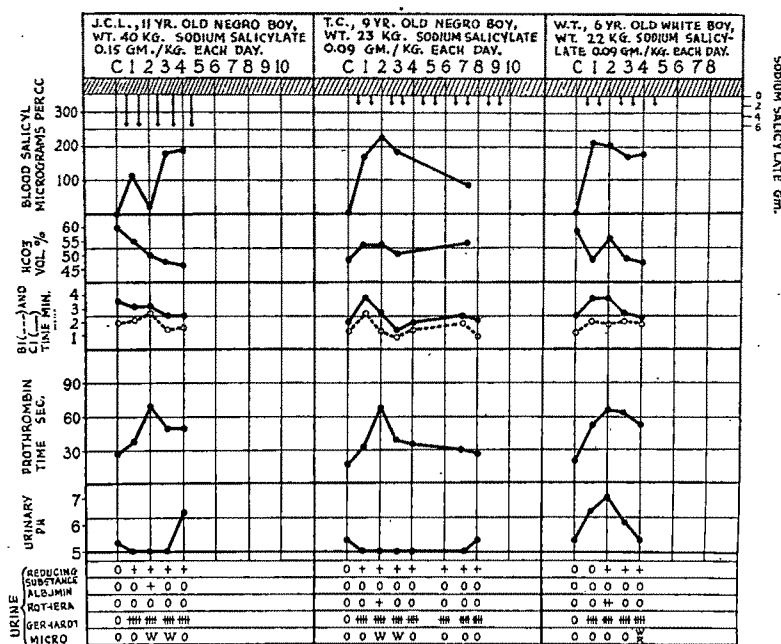


Chart 2.—Effects of administering sodium salicylate to 3 patients at levels of from 0.15 Gm. to 0.09 Gm. per kilogram of body weight per twenty-four hours. See legend under chart 1.

mental period failed to attain the therapeutic level, as did those who received still smaller amounts.

Alkali Reserve.—Five of the 6 subjects showed a moderate but significant fall in the carbon dioxide-combining power of the blood. The drop averaged 12 volumes per cent, which represents, roughly, a 20 per cent decrease in alkali reserve. The effect was slightly more pronounced at the higher levels of dosage, but there was no exact correlation between the amount of salicylate administered and the magnitude of the bicarbonate deficit. Careful observations of rate and depth of respiration were made, and none of the patients exhibited tachy-

the improvement was striking in almost every case. The bleeding and the clotting time were not consistently altered, although there was a tendency toward slight lengthening of both at the height of the prothrombinopenia.

Urinary Changes.—The p_H of the urine was not significantly altered. All subjects excreted small amounts of reducing substance while receiving salicylate. This material was not fermented by a suspension of washed yeast. Urines containing it gave a strongly positive reaction to the Tollens naphthoresorcinol test; this indicates that glucuronides were probably responsible for the reducing action. Albuminuria was noted on 3 occasions in 1 patient and on 1 occasion in

another. White blood cells appeared frequently in the urine, and red cells were seen in 2 instances. Acetone as determined by the Rothera test was noted only 3 times in 38 specimens and disappeared without the employment of special measures. The markedly positive reaction to the Gerhardt test denoted the presence of a salicylate condensation product and could be distinguished readily from a true positive reaction for acetoacetic acid by the purple color, which persisted after preliminary boiling of the urine.

COMMENT

There have been several reports of hemorrhagic complications attending the administration of salicylates, and it is likely that hypoprothrombinemia constitutes one of the mechanisms by which this effect is induced. As Link has pointed out, prothrombin deficiency alone cannot be responsible for the hemorrhages. Other factors, such as vascular dilatation, vascular injury and trauma, undoubtedly contribute their effects. Nevertheless, it is significant that hemorrhages regularly appear in artificially induced salicylate poisoning in rats, hemorrhagic disease of the newborn and hemorrhagic sweet clover disease of cattle, all of which are known to be associated with hypoprothrombinemia. In the light of knowledge concerning the generalized vascular injury occurring in rheumatic fever, the danger of hemorrhagic complications resulting from salicylate therapy in such patients becomes real indeed. Ashworth and McKemie¹⁵ recently observed 2 deaths from hemorrhagic encephalitis in which salicylates appeared to be the lethal factor.

Our studies have shown no correlation between the amount of ingested salicylate or the blood salicyl level and the severity of the hypoprothrombinemia, within the limits of the dosage employed. Prothrombin deficiency was demonstrated on several occasions in the Negro boy, V. R. G., when the blood salicyl level was too low to be detected by chemical test. The explanation for the spontaneous rise in prothrombin in all of the experimental subjects after forty-eight hours is not clear. Apparently this represents a compensatory phenomenon of some sort; but it fails to achieve completely satisfactory restitution of prothrombin level. There are several possible reasons why the boy V. R. G. failed to exhibit this phenomenon. He was receiving a larger dose of sodium salicylate than the experimental subjects. His appetite was

poor and his food intake small, and it is quite possible that he was deficient in vitamin K before salicylate was administered. Klinge¹⁶ has presented evidence for the view that hepatic damage occurs in acute rheumatic episodes even without cardiac failure, and it is conceivable that hepatic dysfunction might occur on this basis, with depression of the prothrombin-forming activity. Such dysfunction, if present, cannot have been severe, since the patient's prothrombin level promptly rose to normal with intensive vitamin K therapy.

The consistent lowering of the alkali reserve which occurred when the sodium salt of salicylic acid was administered in nontoxic amounts to experimental subjects was a rather unexpected finding, in view of the lack of ketosis or of respiratory change. There is no evidence that sodium is excreted more rapidly than the salicylate radical. Guest and his associates¹⁷ have demonstrated that true salicylate intoxication produces a type of alkalosis based on a deficit in carbon dioxide, which is secondary to the hyperventilation induced by the drug. This situation undoubtedly obtained in the first case reported here. However, the fall in alkali reserve in the experimental subjects was unaccompanied by respiratory or urinary changes and can be accounted for most readily by the assumption that accumulation of fixed acids occurred. Lutwak-Mann¹⁸ has shown that administration of salicylates to experimental animals results in early depletion of hepatic glycogen, which may explain the transitory mild ketosis which developed in 3 instances. It would appear that the distortion of the acid-base equilibrium which occurs in acute salicylate poisoning is a complex phenomenon resulting from many factors, viz., primary stimulation of respiration, fixed acid acidosis, ketosis and possibly other changes. The extreme hyperpnea exhibited by V. R. G. was unassociated with ketosis, and without knowing the p_H of the blood, it is impossible to decide whether the low blood bicarbonate was the result of hyperventilation, accumulation of fixed acids or both. It was the impression of all who saw this boy that the intense hyperpnea was out of all proportion to the deficit of carbon dioxide and was almost certainly of central

15. Ashworth, C. T., and McKemie, J. F.: Hemorrhagic Complications, with Death Probably from Salicylate Therapy, *J. A. M. A.* **126**:806 (Nov. 25) 1944.

16. Klinge, F.: Der Rheumatismus: Pathologisch-anatomische und experimentell-pathologische Tatsachen und ihre Auswertung für das ärztliche Rheumaproblem, *Ergebn. d. allg. Path. u. path. Anat.* **27**:1-351, 1933.

17. Guest, G. M.; Rapoport, S., and Roscoe, C.: Clinical and Experimental Studies of Salicylate Poisoning, *Am. J. Dis. Child.* **64**:200 (July) 1942.

18. Lutwak-Mann, C.: The Effect of Salicylate and Cinchophen on Enzyme and Metabolic Processes, *Biochem. J.* **36**:706-728 (Dec.) 1942.

origin. Although we have no data bearing directly on the mechanism of the respiratory disturbance, it seems to us unlikely that changes in temperature and in sensations of heat can fully explain the dramatic hyperpnea. We have observed many patients whose temperatures were artificially raised to 106 F. in the inductotherm, and they showed no such disturbance, although loss of heat from the body is severely curtailed under these conditions.

The appearance of albuminuria and of abnormally formed elements in the urine suggests that salicylates have an irritating effect on the renal parenchyma.

SUMMARY AND CONCLUSIONS

In order to achieve blood salicyl levels of the order of 350 micrograms per cubic centimeter, sodium salicylate has to be administered in amounts which border on toxic doses for children. Evidence is presented which suggests that after an initial twenty-four hour period of large doses the amount given may be reduced without subsequent diminution in blood salicyl level. It is highly desirable, therefore, that the Coburn treatment for rheumatic fever be controlled by repeated estimations of the blood salicyl level in order to attain maximum therapeutic effectiveness with minimal doses.

Moderate as well as large doses of sodium salicylate regularly induce hypoprothrombinemia, which may regress spontaneously to some extent as treatment continues. Large doses of vitamin K appear to prevent the development of prothrombin deficiency and to hasten its restoration to normal levels when the deficiency is already present.

Doses of sodium salicylate as small as 0.09 Gm. per kilogram per twenty-four hours produce a moderate decrease in the alkali reserve not associated with ketosis or with evidence of respiratory alkalosis. This is interpreted as a fixed acid acidosis.

The severe hyperpnea of salicylate intoxication may be unassociated with ketosis and out of all proportion to the bicarbonate deficit. The hyperpnea appears to be the result of central stimulation by the salicyl radical.

When given over a period of several days, sodium salicylate may produce renal irritation and sporadic ketosis.

Sodium salicylate as well as other compounds of salicylic acid should be administered to children with due regard for the hypoprothrombinemia and the acid-base changes which they may produce without overt signs. The concomitant administration of vitamin K is indicated.

2306 Welborn Street.

The Children's Medical Center.

OXYURIASIS

A CLINICAL SURVEY OF 200 CONSECUTIVE CASES OF INFECTION
WITH ENTERIOBIUS VERMICULARIS IN CHILDREN

MAJOR JOHN FLEEK MILLER

AND

LIEUTENANT COLONEL NATHAN H. EINHORN

MEDICAL CORPS, ARMY OF THE UNITED STATES

The development of the cellophane tip, introduced by workers in the National Institute of Health, has provided for the first time a practical laboratory method of diagnosing oxyuriasis.¹ By means of this technic it has been shown that the incidence of this disease is greater than was previously thought.¹ While the method has limitations, as will be demonstrated in this paper, it has proved superior as a means of diagnosis to examinations of stools and of stool concentrates. Brady and Wright used the cellophane tip in studying the symptomatology of this disease in a group of 200 outpatients in Washington, D. C.²

SYMPTOMS COMMONLY ASSOCIATED WITH OXYURIASIS

Textbooks list numerous symptoms attributed to infection with pinworms. The following compilation includes those commonly associated with oxyuriasis by standard texts and by available periodical literature.³

General symptoms: (1) Anemia; (2) malnutrition; (3) anorexia; (4) dark circles under the eyes.

Abnormalities of Blood: Eosinophilia.

From the Pediatric Department of the Medical Service, Gorgas Hospital, Ancon, Canal Zone, Col. Wilmer C. Dreifelbies commanding.

1. Cram, E. B.: Studies of Oxyuriasis: XXVIII. Summary and Conclusions, *Am. J. Dis. Child.* **65**:46-59 (Jan.) 1943.

2. Brady, F. J., and Wright, W. H.: XVIII. The Symptomatology of Oxyuriasis as Based on Physical Examination and Case Histories of Two Hundred Patients, *Am. J. M. Sc.* **198**:367-372 (Sept.) 1939.

3. (a) Brady.² (b) Strong, R. P.: *Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases*, ed. 6, Philadelphia, The Blakiston Company, 1942, vol. 2, p. 1232. (c) Craig, C. F., and Faust, E. C.: *Clinical Parasitology*, ed. 3, Philadelphia, Lea & Febiger, 1943, p. 283. (d) Faust, E. C., in Brennemann, J.: *Practice of Pediatrics*, Hagerstown, Md., W. F. Prior Company, Inc., 1944, vol. 2, chap. 35, p. 8.

Gastrointestinal symptoms: (1) Nausea and vomiting; (2) abdominal pain; (3) sensations produced by worms migrating about the perianal region, such as pruritus ani; (4) excoriation of the perianal region by scratching, secondary dermatitides and infections; (5) rectal colic due to the presence of worms in the rectum; (6) appendicopathia.

Genitourinary symptoms: (1) Enuresis; (2) nocturia; (3) vaginal irritations and discharge.

Nervous symptoms: (1) Restlessness at night; (2) insomnia; (3) lack of cooperation and inattention at school; (4) changes in personality due to a feeling of shame; (5) biting the nails, sucking the thumbs, picking the nose, gritting the teeth; (6) convulsions.

Allergic symptoms: (1) Eczema (allergic); (2) sneezing; (3) asthma.

The principal objects of the present communication are (1) to identify critically the symptoms of oxyuriasis and (2) to offer for the symptoms found a rational explanation based on the pathologic features of this disease.

SUBJECTS IN THE PRESENT STUDY

The patients included in this study were seen either in the pediatric wards or in the outpatient clinic of Gorgas Hospital, Ancon, Canal Zone, from Jan. 1, 1941 to Jan. 1, 1944. Since there is in operation in the Canal Zone a system of federally administered medical care for government employees and their families, no socioeconomic selection existed in this series, and all groups were represented. Racially the patients were white, Negro, Indian, Chinese, Hindu and mixtures of these strains. Since none but the white and the Negro patients presented features of "pure" race, for convenience the patients were classified as white, Negro and mestizo, the last term being used loosely to designate a person of mixed white and other blood.

A total of 200 patients were studied. These were subdivided into two groups: group 1, consisting of 100 patients from the hospital wards, and group 2, consisting of 100 patients from the outpatient clinic.

Sex.—In group 1 there were 55 boys and 45 girls. In group 2 there were 45 boys and 55 girls. Thus sex distribution was equal.

Age.—Group 1 showed no particular pattern of age distribution, the only feature noteworthy in this connection being a low incidence of the infection in infants under 2 years of age. Group 2 showed in addition to this a high incidence between the ages of 2 and 5 years (table 1).

TABLE 1.—*Age of Patients at Time of Diagnosis of Oxyuriasis*

Ages of Patients, Yr.	Number of Patients	
	Group 1	Group 2
1.....	7	4
2.....	16	14
3.....	12	15
4.....	7	13
5.....	7	13
6.....	10	4
7.....	6	7
8.....	8	6
9.....	13	5
10.....	7	4
11.....	1	4
12.....	6	2

Race.—In the pediatric service there are separate wards for Negro and for white children. White children and light-colored mestizos, who are for the most part in the upper pay brackets, are placed in the white ward; Negroes and darker-colored mestizos, mostly in the lower pay brackets, are placed in the Negro ward. Admissions to each ward are about equal. In group 1, 71 per cent were white, 20 per cent mestizo and only 9 per cent Negro. The distribution in group 2 was even more striking, 90 per cent being white, 10 per cent mestizo and none Negro.

Location of Dwellings.—The patients came from dwellings of various types and locations on the Isthmus. In order to determine whether type and location of dwelling had a causal relationship to oxyuriasis, the children were divided into (1) those living in the Canal Zone, where crowding is minimal, sewage disposal excellent and toilet and bathing facilities adequate; (2) those living in the City of Panamá, where poverty and overcrowding are great, sewage disposal fairly good and toilet and bathing facilities inadequate, and (3) those living in the interior of the Republic of Panamá, where there is no crowding but where living conditions are primitive.

In group 1 the distribution was as follows: Canal Zone, 81 per cent; City of Panamá, 14 per cent; interior, 5 per cent. In group 2 it was: Canal Zone, 84 per cent; City of Panamá, 13 per cent; interior, 3 per cent. This observation can be correlated with the racial distribution, since most of the white children lived in the Canal Zone, while most of the mestizos and the Negroes lived either in the City of Panamá or in the interior.

SYMPTOMATOLOGY

Almost all of the patients in group 1 entered the hospital because of diseases unrelated to oxyuriasis. Therefore, it was essential that the patients be studied carefully in order to determine

TABLE 2.—*Symptoms Encountered in 200 Children Infected with Enterobius Vermicularis*

	Percentage of Patients	
	Group 1	Group 2
Local symptoms and signs:		
Worms on anal region.....	13	59
Pruritus ani and associated sensations.....	0	17
Vaginitis, nonspecific.....	1	1
Symptoms secondary to local discomfort:		
Wakefulness at nights.....	1	7
Enuresis.....	0	3
Burning on urination.....	1	0
Nocturia.....	0	1
Pain in groin caused by inguinal adenitis secondary to vulvovaginitis.....	1	0
"Nervous" symptoms probably secondary to disturbed sleep and general discomfort:		
Anorexia.....	6	7
Failure to gain weight.....	6	1
Irritability, fretfulness, restlessness.....	3	3
Lethargy.....	2	1
Grimacing, facial tics.....	1	1
Thumb sucking.....	0	1
Gritting of teeth.....	0	1
Headache.....	0	1
Gastrointestinal symptoms probably due to irritation by enterobii within the gastrointestinal tract:		
Abdominal pain.....	11	13
Nausea and vomiting.....	5	4
Diarrhea.....	2	1

whether the presenting symptoms were due to parasitic infection or to unrelated disease.

In the analysis of group 1 a liberal attitude was maintained. Conditions which could not be explained by unrelated disease were listed as symptoms of pinworms, even though they are frequently seen in children without pinworm infection. In group 2 the problem was simpler, since oxyuriasis was often the only disease present. The symptoms found, with the percentages of patients showing them in both groups, are listed in table 2.

Five patients in group 2 had fever of undetermined cause. This incidence is no greater than is to be expected in the tropics and is probably unrelated to infection with pinworms.

Convulsions were present in 2 patients in group 1; both instances were accounted for by

meningismus occurring at the onset of acute suppurative otitis media. No patients had convulsions as a manifestation of oxyuriasis.

Seventy-five and 50 per cent of groups 1 and 2 respectively were free from subjective symptoms attributable to oxyuriasis. Thus, in 125 patients the presence of the infection was determined either by means of cellophane tips or by the mother or nurse seeing the worms.

TABLE 3.—*Hemoglobin Values in Oxyuriasis Contrasted with Values Obtained in a Series of 30 Control Patients*

Hemoglobin, per Cent	Percentage of Patients		
	Group 1	Group 2	Control Group
50.....	0	0	3
55.....	3	0	3
60.....	9	4	10
65.....	19	39	25
70.....	49	43	42
75.....	17	14	17
80.....	3	0	0

LABORATORY CONSIDERATIONS

Hemoglobin.—Estimations were done by the Tallqvist technic in most instances. All 100 patients in group 1 and 30 patients in group 2 had hemoglobin determinations. There was no significant difference in hemoglobin level between the children with oxyuriasis and a control group (table 3). The control group consisted of 30 children admitted to the surgical service with simple uncomplicated fractures but free from medical disease.

Erythrocyte Counts.—As with the hemoglobin levels, the erythrocyte counts of the children

TABLE 4.—*Erythrocyte Counts in Oxyuriasis Contrasted with Values Obtained in a Series of 30 Control Patients*

Erythrocyte Counts	Percentage of Patients	
	Group 1	Control Group
Less than 3,000,000.....	3	0
3,000,000 to 3,500,000.....	21	20
3,500,000 to 4,000,000.....	40	37
4,000,000 to 4,500,000.....	20	24

with oxyuriasis were not essentially different from those of the controls (table 4). Here only group 1 has been considered, since few counts were done for group 2.

Leukocyte Counts.—Leukocytes of the 100 patients of group 1 only were considered. All deviations from the normal were caused by the unrelated presenting disease; the count varied from 3,500 to 18,500. Only four counts were

above 12,000, and these were explicable by infections other than oxyuriasis. The mean was between 6,500 and 7,000.

Differential Leukocyte Counts.—The percentage of neutrophils varied between 20 and 90, with an average of 59.3. The percentage of lymphocytes and monocytes combined varied between 10 and 80, with an average of 39.3.

Special consideration was given to the eosinophils, since they have been mentioned as diagnostic in oxyuriasis (table 5). Todd and Sanford⁴ stated that the normal number of eosinophils varies from 1 to 4 per cent. By this standard, 7 patients in group 1 showed eosinophilia. Two of these had asthma; thus 5, or 5 per cent, had eosinophilia presumably due to oxyuriasis. In group 2, eosinophilia was present in 13 patients^{4a} of a total of 34. One of these patients was asthmatic; hence 12 patients, or 35 per cent, had eosinophilia presumably due to oxyuriasis.

TABLE 5.—*Occurrence of Eosinophilia in Oxyuriasis*

Eosinophils, %	Percentage of Patients	
	Group 1 (100 Patients)	Group 2 (34 Patients)
None.....	54	35
1.....	14	3
2.....	11	14
3.....	12	9
4.....	2	6
5.....	3	9
6.....	2*	9†
7.....	1	9
8.....	0	3
18.....	1*	0

* Includes 1 patient with asthma (1%).

† Includes 1 patient with asthma (3%).

Methods of Diagnosis.—In 13 per cent of group 1 the diagnosis was made by seeing worms on the perianal region. Although examinations were done on the stools of all patients in this group, in only 1 case was diagnosis made by finding ova in the stool. Cellophane tips yielded positive results in 95 and negative in 5 per cent of the cases. Worms were seen in 59 patients of group 2. For 19 of the 59 tips were done with 13 positive and 6 negative results. For the remaining 40 patients the diagnosis was made by tips alone, without worms being seen. Twenty examinations of stools were done for the patients of group 2, and all gave negative results.

4. Todd, J. C., and Sanford, A. H.: *Clinical Diagnosis by Laboratory Methods*, ed. 10, Philadelphia, W. B. Saunders Company, 1943, p. 278.

4a. Ed. NOTE.—The percentages in the column for group 2 in table 5 seem to account for only 33 (instead of 34) patients and to show only 12 with eosinophilia. Because the authors are in military service, we were unable to send them a proof and get this discrepancy explained or corrected.

TREATMENT

In general, three types of treatment were tried here: 1. Administration of gentian violet in enteric-coated capsules. This was given in doses of from 0.25 grain (0.015 Gm.) to 1 grain (0.06 Gm.) three times a day twenty minutes before each meal for two periods of eight days each, interrupted by a rest period of seven days. This treatment was used only for children old enough to swallow the capsules intact. 2. Administration of quassia enemas. Rectal injections of 2 to 3 ounces (60 to 90 cc.) of a strong infusion of quassia chips were given, followed in twenty minutes by a soapsuds enema. This routine was repeated on alternate days for two months. 3. Administration of tetrachloroethylene. This medicine was given in a single dose preceded the night before by a preparatory purgative of magnesium citrate. Treatment was administered at 8 a. m. with another dose of magnesium citrate and food withheld until supper.

Irrespective of the type of therapy, all mothers of patients were given specific instructions regarding prevention of self reinfection in their children. The finger nails were ordered cut and ammoniated mercury ointment applied to the fingers and the anal region twice daily. Only the tetrachloroethylene was administered in the hospital and in the outpatient clinic. Gentian violet and quassia enemas generally were given at home by the parents.

RESULTS OF TREATMENT

Evaluation of treatment is difficult because of inadequate follow-up care. Furthermore, there is no perfectly reliable method of ruling out oxyuriasis. In some patients as many as five or six negative cellophane tips were followed by a positive tip, and such occurrences introduced the question of reinfection. The wide distribution of the ova, as demonstrated by Faust^{3d} makes reinfection from outside sources a possibility. Criteria used here for determining the success of treatment were: (1) absence of visible worms on the perianal region, (2) cessation of symptoms and (3) where possible repeated negative results with cellophane tips.

Thirty-six patients of group 1 were treated with gentian violet, vomiting occurring in 2 instances. Tetrachloroethylene was given to 9 patients. Anorexia, vomiting, listlessness and diarrhea occurred in 1 patient each. Thus, half of the hospital patients given tetrachloroethylene showed toxic symptoms. Quassia enemas were given to 15 younger children and infants. Ab-

dominal pain was encountered in 1 so treated. Follow-up care for group 1 was too inadequate to permit evaluation of the efficacy of the treatment.

Forty children of group 2 were treated with gentian violet, 26 with quassia enemas and 10 with tetrachloroethylene. Twenty-four received at one time or another several types of therapy, the changes being made because of failure of the first treatment tried.

Of the 40 patients of group 2 who were treated with gentian violet, 14 returned for follow-up care. Of these 14 patients 7 had originally had symptoms and 7 had been without symptoms; in 13 worms had been seen by the mother. Of the 7 patients who had had symptoms there were complete success with 6 and failure with 1, as judged by disappearance of symptoms and of visible worms together with between one and four negative results with tips. Of the 7 patients who had been without symptoms worms were seen in 6 and for 1 the diagnosis was made by means of a tip. All were successfully treated as judged by similar criteria. However, in the treatment of 5 other patients given gentian violet the use of the drug had to be discontinued because of vomiting. Furthermore, younger patients cannot be treated with this drug as outpatients, because they will not willingly swallow the capsules whole and mothers cannot be trusted to insert them into the esophagus.

Of the 26 patients treated with quassia, 10 returned for follow-up care. Of these 10, 6 were originally symptomatic and 4 were asymptomatic. All showed symptomatic relief, although in 2 there was continued infection, as indicated by the persistence of worms in 1 child and by a positive tip in the other.

Eight patients given tetrachloroethylene returned for follow-up care. Six of these were symptomatic. In none was there relief from symptoms, and all but 2 continued to have visible worms and positive results with tips and visible worms.

Although numerically too small for conclusive decisions, these series have been presented because they show results of therapy under typical office conditions.

COMMENT

Racial Distribution.—Several points in this analysis merit comment. First is the failure to find infection in the Negroes and mestizos in the proportion which would be expected in the face of low standards of cleanliness. Cram also reported a much higher incidence of oxyuriasis in white persons than in Negroes in Washing-

ton.¹ To date no satisfactory explanation of this seemingly paradoxical observation has been advanced.

Age Distribution.—As regards the age of patients, the relatively even distribution in group 1 seems to indicate that after 2 years of age the infection rate is fairly even, with probably a gradual fall as adult life is approached. The high incidence between 2 and 5 years of age in group 2 may be due to the facts that mothers still observe their children closely at these ages and that such symptoms as pruritus ani are more obvious in the uninhibited child.

Symptoms.—In a critical review of the symptoms seen in these cases, it seems that such local disturbances as pruritus ani, vaginal irritations and local secondary infections can be attributed definitely to oxyuriasis. A second group of symptoms, consisting of wakefulness at night, pain on urination, nocturia and possibly enuresis, can be attributed to the discomfort of vaginitis and pruritus ani. The "nervous" symptoms should be considered in a third group: Anorexia with consequent failure to gain weight, irritability, lethargy, nail biting, thumb sucking, gritting of teeth, headache, tics, etc., while frequently seen in uninfected children, are all aggravated by disturbance of sleep and by general discomfort. Thus they may be symptoms of oxyuriasis when seen in an infected child. This psychogenic explanation seems more rational than that of Craig and Faust^{3c} and of Strong,^{3b} who considered these manifestations reflex reactions to exposure of sympathetic nerve endings by erosion of the cecal mucosa. These writers also mentioned convulsions as a symptom. Not a single instance was encountered in this series. Nor does the theory that convulsions can result from reflex irritation originating in an ulcerated mucosa appear tenable, because convulsions are rarely encountered in amebic dysentery and in ulcerative colitis. In the absence of irrefutable proof, pinworms should not be considered a cause of convulsions in children.

Gastrointestinal symptoms, such as abdominal pain, diarrhea, nausea and vomiting, can be explained readily as the result of irritation of the intestinal mucosa, as was demonstrated by Faust.^{3a} The symptom of abdominal pain was seen in both group 1 and group 2 with considerable frequency. In most instances it was vague, and the patients did not show the picture associated with abdomens requiring surgical intervention. However, since the association of pinworms with appendicitis has been so frequently discussed, it was felt advisable to investigate

separately from the general group a series of patients on whom appendectomies were performed. Thirty-five appendectomies were performed on children in Gorgas Hospital during the three years covered by this survey.⁵ Of the 35 patients who were considered clinically to have appendicitis and who were therefore operated on, 7 had pinworms in the appendix. Of the 7 appendixes, 5 were classified pathologically as acutely catarrhal and 1 as fibrotic; 1 showed no pathologic manifestations other than the presence of enterobii. Of the 28 appendixes not containing pinworms, 10 were suppurative, 1 acutely catarrhal, 1 fibrosing, 1 gangrenous and 5 normal. It seems justifiable in the face of this 20 per cent incidence and of the associated pathologic findings to consider that enterobii can and do cause catarrhal inflammation of the appendix. However, there is no evidence in this series that pinworms alone can cause the suppurative form of the disease.

Whether some of the patients in this series who complained of vague abdominal pain had enterobii on the appendix it is impossible to say. In any case, the possibility that pinworm therapy may obviate the necessity for appendectomy furnishes an excellent reason for searching assiduously for enterobii in patients complaining of vague abdominal pain. In the present series this symptom frequently yielded to pinworm therapy.

There was no gross interference with the nutritional state of the patient, as was seen in ascariasis, nor was there evidence of systemic disturbances produced by absorption of by-products or of toxins. Allergic symptoms, such as asthma and eczema, did not occur with unwarranted frequency, and when present they did not respond to worm therapy. Moderate improvement in appetite and in general well-being probably attributable to the comfort and happiness of undisturbed rest, was noted after treatment.

The patients in the present study were not considered anemic. Hemoglobin levels and erythrocyte counts both in the children infected with enterobii and in the controls seem low to one unfamiliar with tropical pediatrics. Low findings are, however, commonplace in well Panamanian and Canal Zone children. These children not only look and act normal but resist attempts to raise the hemoglobin by administration of iron or other hematinics. A slight eosinophilia was apparently present in some of the patients, but

5. Dr. H. K. Tuttle, Chief of the Surgical Service and Col. L. B. Bates, Chief of Laboratories, gave permission to use this material.

was too inconstant and slight to be of diagnostic value.

A suggested revision of the symptomatology of oxyuriasis, based on the preceding observations and on the well established findings in current literature, is presented:

A. Local symptoms: (1) Pruritus ani and associated sensations; (2) vaginal and perianal irritations and secondary infections, mostly due to scratching.

B. Symptoms secondary to local discomfort: (1) Wakefulness at night; (2) genitourinary disturbances such as nocturia, burning on urination and possibly enuresis, and any other symptoms occasioned by nonspecific vaginitis.

C. "Nervous" symptoms, secondary to disturbed sleep and general discomfort: There is nothing specific in this group, and any behavior or personality difficulty certainly can be aggravated, if not caused, by severe perianal itching. Anorexia, irritability, lethargy, thumb sucking, tics and headaches are among these symptoms but do not constitute all of the possibilities.

D. Gastrointestinal symptoms, probably due to irritation by enterobii within the gastrointestinal tract: (1) Abdominal pain, including appendicopathia; (2) nausea and vomiting, and (3) diarrhea.

E. Pathologic changes in the blood: Eosinophilia.

Until further proof is presented, it would seem advisable to drop from the symptomatology of oxyuriasis anemia, malnutrition of any marked

degree, convulsions and all allergic manifestations. When such symptoms are present, the mere finding of pinworms does not explain them adequately.

Diagnosis.—There is to date no perfectly satisfactory method for the diagnosis of pinworm infection. The introduction of the cellophane tip is a great advance. However, careful observation of the anal region of the patient by the mother or a nurse, especially at night, remains an important diagnostic method. By this means, it is possible to diagnose infection at times when cellophane tips fail to reveal it. Examination of stools and of stool concentrates is of little value. The scotch tape method described by Von Hope⁶ is under trial in this hospital at present.

Treatment.—Treatment was not entirely satisfactory. Gentian violet appeared to be the best of the methods tried here. However, it can be used only with older children, who, after all, do not constitute a majority of the patients with symptoms. Occasionally, even older children cannot tolerate the drug because of vomiting. Quassia enemas proved valuable, especially for infants and younger children. This method was troublesome for the mothers, and while it relieved symptoms, it did not always cure the infection. Tetrachloroethylene as used in this clinic was of no value.

6. Von Hope, F. H.: An Improved Method of Demonstrating Ova of *E. Vermicularis*, J. A. M. A. **125**:27 (May 6) 1944.

GENERALIZED CUTANEOUS MONILIAL INFECTION

ALBERT STRICKLER, M.D.

Medical Director, Hersch-Razel Research Foundation; Medical Director,
Skin and Cancer Hospital

PHILADELPHIA

It is the purpose of this paper to report an instance of generalized cutaneous monilial infection in a young child. Survey of the literature shows comparatively few instances of this infection, the largest series being that of F. W. Schlutz,¹ who studied 5 instances of generalized

generalized thrush into two types. The first is the chronic septic form, with lesions of the buccal mucous membrane and extensive angina. It involves the gastrointestinal tract, including the anus, and the female genitalia. Often there is more or less involvement of the lungs; the liver



Fig. 1.—Scalp of a 2 year old girl with monilial infection.

systemic thrush during twenty-five years of pediatric practice. Schlutz roughly classified

From the Skin Clinic, The Skin and Cancer Hospital of Philadelphia.

1. Schlutz, F. W.: Systemic Thrush in Childhood, J. A. M. A. **105**:650 (Aug. 31) 1935.

and the kidneys are the abdominal organs most often affected. The second type consists of the exceedingly chronic forms, with cutaneous lesions affecting the extremities, the nails, the nail bed and, in isolated patches, the trunk. In this type of thrush the cutaneous lesions are dry, scaly

and crusted and characterized by only slight itching except when the interdigital spaces are involved. At no time is the inflammatory reaction of the skin severe. Vesicles are observed. All the 5 instances of generalized moniliasis observed by Schlutz were of the chronic septic type. The interesting features of these cases are a dwarfing effect in 2 patients and alopecia in 3. Sepsis, when it occurred, was rapid and generalized, and treatment proved futile.

testinal involvement with recovery. Pels and his associates⁴ described an interesting case of monilial infection in a boy, with involvement of the face, scalp, ears, neck, upper part of the chest, thumb and mouth, which lasted many years, proved resistant to treatment and, was finally fatal. Downing and Hazard⁵ reported an instance of cutaneous moniliasis with oral thrush in a white boy 15 years of age. For eighteen months there was a horny eruption on the face.



Fig. 2.—Arms and hands of a 2 year old girl with monilial infection.

J. F. Schamberg² reported an instance of thrush of the mouth in a 6 month old infant, with extensive cutaneous lesions and death. M. Goldring³ reported an instance of thrush complicated by acute polyarthritis and extensive gastroin-

Eight years prior to this he had suffered from canker sores, and two years before a nail had become painful. On his admission to the hospital there were lesions on the cheeks and the lips and a blackish yellow lesion on the nose. There was little inflammation, and after the lesions healed

2. Schamberg, J. F.: Report of Case of Extensive Fatal Thrush with Involvement of the Skin and Secondary Infection of the Mother's Breasts, *Arch. Pediat.* **32**:617, 1915.

3. Goldring, M.: Thrush Complicated by Acute Polyarthritis in an Infant, *J. A. M. A.* **76**:724 (March 12) 1921.

4. Pels, I. R.; Dresel, I., and Salinger, R.: An Unusual Eruption Due to an Organism of the Monilia Group, *Arch. Dermat. & Syph.* **14**:280 (Sept.) 1926.

5. Downing, J. G., and Hazard, J. B.: Cutaneous Moniliasis Associated with Oral Thrush, *Arch. Dermat. & Syph.* **31**:636 (May) 1935.

pitted scars remained. The patient ultimately died of tuberculous pneumonia.

REPORT OF A CASE

N. C., a white girl aged 2 years, was brought to the clinic with the history that in the past summer, for the second time, she had broken out with a rash. Examination of the skin showed marked matting of the hair of the scalp. The crusts were yellowish, and the hair grossly showed no abnormality. There were no breaking off of the hair, no hair stumps, no scaling and no patches of alopecia. The picture of the scalp simulated that in neglected pediculosis capitis with secondary proderma, except that here marked impetiginization was absent. The forehead, arms, hands and thighs presented a uniform picture of circinate lesions with clear or scarcely scaly centers and crusted, elevated, scaly borders. Here and there appeared evidence of a vesicular element at the border. Inflammation was noticeably absent, and there was only moderate subjective discomfort. The nails of the hands and feet were involved and presented loss of transparency, a dark yellowish brown color, thickness and fragility. A mild degree of paronychia was present. The picture presented was quite at variance with the chronic monilial onychia seen in adults. The buccal mucous membranes were normal, and evidence of perlèche and of erosio interdigitalis blastomycetica was absent. There was no vaginal or anal involvement.

Physical examination showed an otherwise normal child, in good health, well nourished and with no gastrointestinal symptoms. The parents were healthy. The mother did not complain of leukorrhea.

Laboratory Studies.—Direct examination of the crusts of the scalp, of the finger nails and of the cutaneous

lesions showed numerous mycelial threads and groups of spores. The mycelium showed little branching. Material from the various affected areas was inoculated on Sabouraud's medium. It was studied by Dr. Randle C. Rosenberger, who submitted the following report: "The cultures from the skin, nails and eyebrows show a whitish, smooth, glistening growth, and spreads made from each of these growths show oval, spheroid and elongated budding cells. In my opinion the organism corresponds morphologically and culturally with *Monilia albicans*." Inoculation of gelatin with material from the cutaneous lesions and the scalp produced liquefaction of the medium, while in dextrose bouillon formation of gas was demonstrated. Dr. George M. Lewis studied the culture and confirmed the opinion that the organism was *Monilia albicans*.

No organisms could be demonstrated in the urine, and the blood count was normal. The Wassermann and Kahn reactions were negative.

Treatment.—After application of 50 per cent alcohol all of the cutaneous eruptions disappeared, but they recurred later. An iodine ointment prescribed for the scalp was also used on the cutaneous relapsing lesions; it proved beneficial.

SUMMARY

The exceedingly chronic form of generalized moniliasis occurred in a young child. The cutaneous lesions were arcuate in form with but insignificant inflammatory reaction, and caused only slight subjective discomfort.

327 South Sixteenth Street.

PRIMARY TUBERCULOSIS

EFFECT OF UNRESTRICTED ACTIVITY ON PROGNOSIS

MILTON I. LEVINE, M.D.

NEW YORK

Although the pathologic changes characteristic of the primary complex of tuberculosis are fairly well understood at the present time, the indications for treatment and the methods of treatment are still subjects of controversy.

Until recent years all children who showed positive reactions to the tuberculin test, even in the absence of signs or symptoms of tuberculosis activity, were given special attention. Increased rest was advised, school classes in the open air were instituted and preventoriums were established throughout the United States. Within the past few years preventoriums and treatment in the open air for children who react positively to the tuberculin test have for the most part been discontinued, for it is now generally accepted that a positive reaction to tuberculin is by itself no indication for added care except that occasional roentgenograms should be made. It has also been recognized that a child with only a positive reaction to tuberculin is no menace to other children.

On the other hand, the treatment of a patient with tuberculous infiltration of the parenchyma of the lungs during the active phase of the primary complex as evidenced by roentgenograms is still subject to dispute. Many physicians continue to advise rest in bed during the infiltrative phase of the primary complex in the hope that recovery will be hastened and complications avoided. Other physicians feel that the course of a primary tuberculous infection and its subsequent outcome are not modified by treatment.

Wallgren¹ expressed the opinion that "the child should generally be kept in bed until the sedimentation rate returns to normal. . . . On the average the necessary period of rest in bed is from four to six weeks after the fever has subsided. The child should then be allowed up for short intervals, the duration of the intervals

being determined by the temperature and the results of the sedimentation tests." Wallgren further wrote: "It is generally advisable in the case of children who have not reached school age to insist on two or three hours' rest every day during the first year and one hour daily during the second year after the onset of the primary tuberculosis in addition to the midday rest which every baby should obtain. . . . In addition to the rest in bed during the acute stage of primary tuberculosis, the treatment requires an open air cure as similar as possible to that of the sanatorium routine."

Myers,² on the other hand, stated that "it makes no difference whether children who have the first infection type of tuberculosis are given strict rest in bed in a sanatorium and even have collapse therapy instituted, whether they are placed in a special school or whether they remain at home under the same conditions as normal children should have. The course of the disease is the same." Myers would treat the child during the febrile stage "just as when fever is caused by other infections such as influenza." He minimizes the importance of the sedimentation rate.

In view of these diverse opinions, it was felt that a study of a fairly large group of children, observed during the parenchymal involvement of a primary complex and followed for a period of years, would prove of value.

EXPERIMENTAL MATERIALS AND METHODS

The data were accumulated during the course of an investigation on tuberculosis in childhood. The study was carried on from 1926 to 1942 in the city of New York by the Bureau of Laboratories of the Department of Health. More than 1,000 children from tuberculous homes were followed during and after the first year of life. A large number of these children were brought regularly to the clinics for roentgenograms and tuberculin tests. All children were referred from tuberculosis clinics and hospitals in the city of New York.

The basis for acceptance of lesions as demonstrating parenchymal infiltration by tuberculosis was serial roentgenograms which revealed calcification on resolu-

Aided by a grant from Mead Johnson and Company. From the New York Hospital; the Department of Pediatrics, Cornell University Medical College, and the Bureau of Laboratories, New York City Department of Health.

1. Wallgren, A.: *Pulmonary Tuberculosis in Children*, New York, Thos. Nelson & Sons, 1939, pp. 177 and 142.

2. Myers, J. A.: *Tuberculosis in Children and Youth*, Springfield, Ill., Charles C Thomas, Publisher, 1938, p. 169.

tion in a child who reacted positively to the tuberculin test.³ The routine dose of tuberculin for intradermal tests was 0.1 mg. The reactions were read by pediatricians on the staff or by specially trained nurses.

During the course of the study gross parenchymal lesions of tuberculosis developed in 90 children. Fifty-eight were under 1 year of age when parenchymal involvement was first seen. The onset of the primary complex in 27 of these 58 infants was in early infancy. This group was listed as nonambulatory during the primary involvement, since death occurred or the evolution of the primary complex was complete or almost complete before the infants reached 12 months of age. All of the remaining 63 patients, with the exception of 3, were ambulatory during the course of the primary complex. No effort was made to restrict their activities unless the fever rose to over 101 F. by rectum. All the children were followed for at least five years from the time the pulmonary parenchymal involvement of the primary tuberculous complex was first visualized.

This paper reports the mortality and morbidity due to tuberculosis in terms of the complications as evidenced by roentgenograms, of children with gross pulmonary infiltration, who were permitted to remain ambulatory throughout the course of the primary complex.

culous, and the patient later died of the infection. These 3 children were hospitalized because of difficult situations in the home.

TABLE 1.—Deaths and Complications in Patients with Gross Parenchymal Involvement of Lungs with Reference to Age at Which First Infection Was Acquired

	Number	Deaths from Tuberculosis	Complications
Up to 12 months of age.. (nonambulatory)	27	16	1 (tuberculosis of hip)
Over 12 months of age... (ambulatory)	60	4	2 (1, tuberculosis of cervical and mesenteric nodes and tuberculous dactylitis; 1, tuberculosis of cervical nodes)
(Hospitalized).....	3	1	1 (tuberculosis of spine)

In view of the opinion that young infants are less resistant to the tubercle bacillus than are

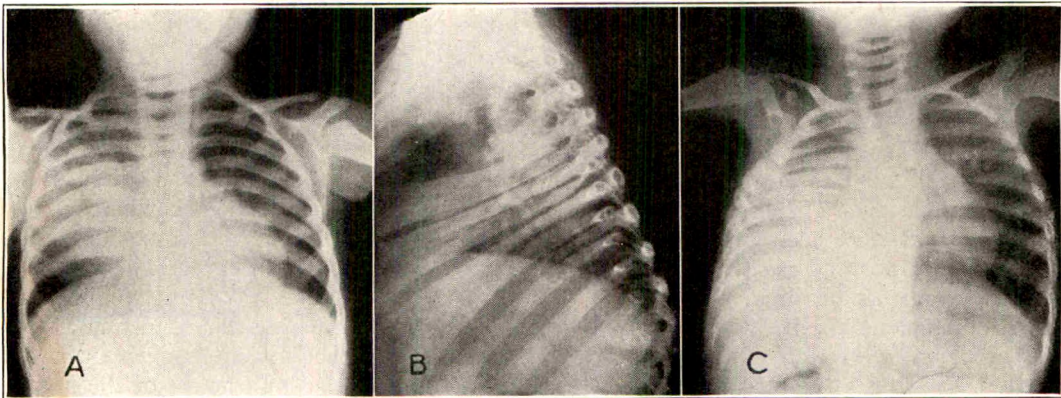


Fig. 1.—Hospitalized patient (C. R.) with complication. A, age 13 months; infiltration in right midlung field. B, age 23 months: kyphosis at junction of thoracic and lumbar vertebrae. C, age 23 months: large psoas abscess.

RESULTS

Of the 90 children followed in this study, 27 acquired their first tuberculosis infection and went through the most active phase of the primary complex, as evidenced by roentgenograms, before they had reached their first birthday. In this group of 27 nonambulatory infants, 16 deaths and 1 subsequent complication (tuberculous disease of the hip) occurred.

On the other hand, of the 60 children who were definitely ambulatory during the period of primary parenchymal involvement 4 died from tuberculosis and only 2 had minor complications. Only 3 of the children over 1 year of age were hospitalized when the pulmonary infiltration was visualized; the spine of 1 of these became tuber-

TABLE 2.—Deaths and Complications in Patients with Tuberculosis with Reference to Month at Which Parenchymal Involvement of the Lungs Was First Detected

Age Parenchymal Lesion First Seen, Months	Number of Cases	Deaths from Tuberculosis	Complications
1	0	0	
2	1	1	
3	3	3	
4	5	2	
5	3	0	Tuberculosis of knee in 1 patient
6	5	2	Tuberculosis of cervical nodes in 1 patient
7	10	2	
8	5	2	
9	5	1	
10	6	2	
11	7	3	
12	8	2	
Indefinite (under 12 mo.)	1	0	
Over 12 mo.	31	1*	

* The child went through the primary complex without complication; a tuberculous reinfection occurred at 7 years.

3. The roentgenograms were read by Dr. John Carty, Professor of Roentgenology, Cornell University Medical College.

older infants, the cases were studied with reference to the month at which parenchymal involvement of the lungs was first detected. The results of this study are presented in table 2.

Of the 59 patients in whom pulmonary infiltration was first visualized during the first twelve months of life, 20 died from tuberculosis, a mortality of 33.9 per cent. Of the 31 patients in whom infiltration was first seen after they

primary focus was seven and seven-tenths months and that the time to complete calcification averaged twenty-one and one-tenth months. Wallgren, who advised rest in bed for children with active primary tuberculosis, states¹ that "the first trace of calcification is generally seen after about a year or a year and a half, and after the lapse of from two to three years the primary complex has, as a rule, become com-

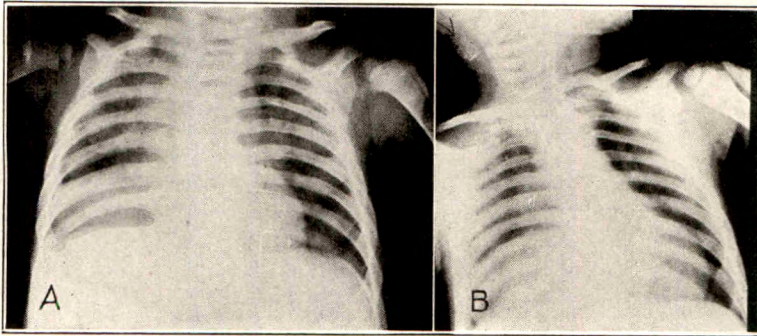


Fig. 2.—Ambulatory patient (J. Z.) with complication. *A*, age 12 months: marked consolidation in lower lobe of right lung; mediastinum widened. *B*, age 23 months; definite calcification of cervical nodes.

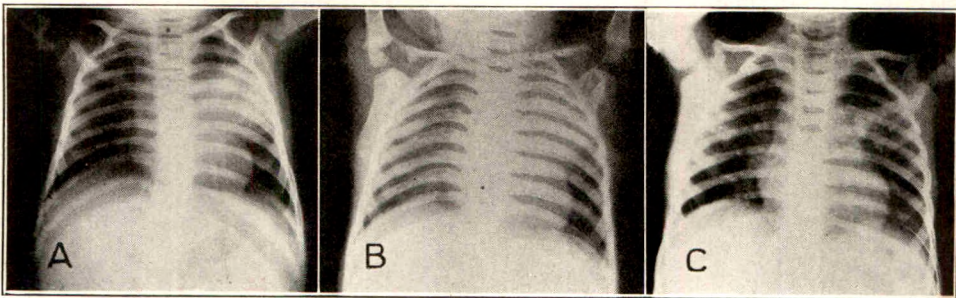


Fig. 3.—Ambulatory patient (M. F.) without complications. *A*, age 10 months: massive infiltration in upper lobe of left lung. *B*, age 14 months: massive infiltration in upper lobe of left lung still present. *C*, age 38 months: large calcification of left hilus and large calcified left hilar node.

were 12 months of age, only 1 died. Death in this instance occurred from a reinfection in a child of 7 years who had successfully passed through the primary complex three years before death.

COMMENT

In spite of the fact that 60 young children with roentgenographic evidence of primary pulmonary tuberculous infiltration were permitted to be ambulatory during the acute phase of the primary complex, there was no evidence that this circumstance was in any way detrimental. Not only was there comparatively little mortality from tuberculosis, but there was no indication that the course of the disease was lengthened or that complications resulted.

In this group of 60 infants and young children, a careful study of roentgenograms revealed that the average time from parenchymal infiltration to earliest signs of calcification of the

pletely calcified." If it is assumed that the virulence of the tubercle bacilli in Sweden is similar to the virulence of those responsible for most of the morbidity in the city of New York and that the general course of infection is similar in the two places, it would appear that there was no lengthening of the period of active infection in patients ambulatory during the primary complex.

An analysis of the histories of the children in this series demonstrates that the age of the children at the time of infection rather than the method of treatment is the important factor in mortality from primary tuberculosis in early childhood. The high mortality during the first year has been reported by numerous investigators, and the opinion has been expressed that the high degree of susceptibility at this age is in all probability due to the intimate contact of infants with parents at that time as well as to

the inability of young infants to form adequate antibodies.

In the study of patients reported on in this paper there is added evidence of the importance of intimate contact. Of the 59 infants in whom parenchymal pulmonary lesions developed before they had reached 12 months of age, 19 were

TABLE 3.—*Contacts and Mortality Due to Tuberculosis of Infants in Whom Pulmonary Tuberculosis Infiltration Developed Before 12 Months of Age*

Exposed to	Total	Deaths from Tuberculosis	Mortality Due to Tuberculosis, per Cent
Mother.....	19	10	52.6
Father.....	28	6	21.4

way alter the course of the primary complex. A comparison with the studies reported by Wallgren furnished no evidence that rest in bed decreases the activity of the process, prevents tuberculous complications or lowers the mortality from tuberculosis.

SUMMARY

The indications for treatment and the methods of treatment of the primary complex of tuberculosis are still subjects of considerable controversy.

In the course of a study on tuberculosis in childhood, 90 infants were observed before, during and after their primary complex.

Twenty-seven of these infants had the primary pulmonary lesion with perifocal infiltration and

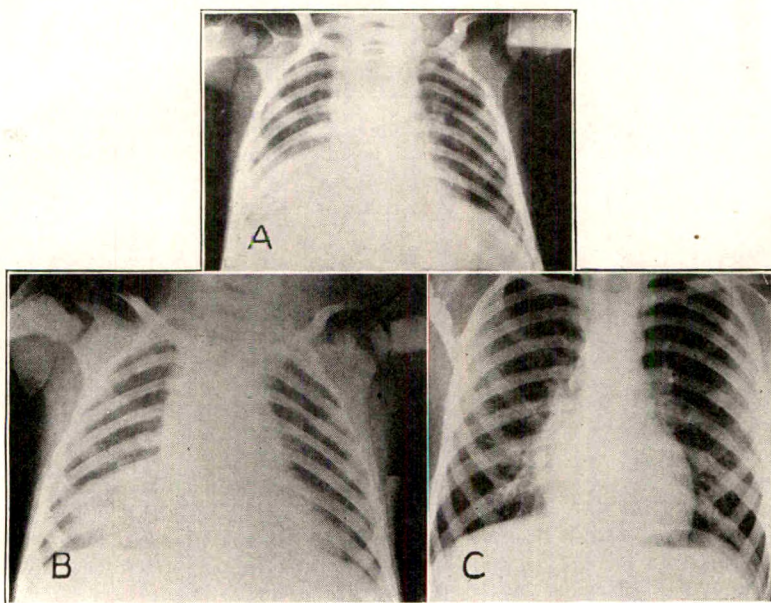


Fig. 4.—Ambulatory patient (S. K.) without complications. A, age 12 months: massive consolidation in lower lobe of right lung; mediastinum widened. B, age 22½ months: consolidation still massive but resolving; mediastinum still widened. C, age 8½ years: dense calcification in lower lobe of right lung of cardiac border; calcified right hilar node.

exposed to their mothers and 28 to their fathers. But, as is seen from table 3, 52.6 per cent of those exposed to mothers died of tuberculosis as against 21.4 per cent of those exposed to fathers.

It is apparent, then, that infants exposed to mothers with active tuberculosis are much more prone to die of the disease than are those exposed to fathers. This is probably due in large part to the extremely close contact of infants with their mothers.

My results, based on the careful observation of 90 children exposed to and infected with the human tubercle bacillus, would seem to indicate that rest in bed does not in any demonstrable

went through the active phase of the primary complex before they were 12 months of age. These infants were classified as nonambulatory. Of the 27 infants 16 died from tuberculosis and 1 had a complication, tuberculosis of the hip.

All except 3 of the 63 remaining infants were ambulatory throughout the primary complex in spite of the size of the pulmonary infiltration. Of these 60 ambulatory patients only 4 died from tuberculosis and only 2 had complications—tuberculosis of the cervical nodes in 1 instance and multiple hematogenous lesions in the other.

Of the 3 hospitalized patients 1 died from tuberculosis and 1 had a complication—tuberculosis of the spine.

There was no evidence that rest in bed influenced in any way the course of the primary complex or reduced the incidence of complications and no evidence that lack of rest in bed was in any way detrimental.

It would appear that the age of the child at the time of infection rather than the method of treatment was the important factor in determining prognosis.

In the cases reported, it was apparent that contact with a tuberculous mother during the

first year was much more dangerous than contact with a tuberculous father. This fact is probably the direct result of the intimate contact of infants with their mothers.

In my opinion, rest in bed during a primary infection with tuberculosis should be limited only to the period of elevation of temperature, as would be advised in the treatment of any febrile condition during childhood.

1049 Park Avenue.

ILLNESS HISTORY AND PHYSICAL GROWTH

II. A COMPARATIVE STUDY OF THE RATE OF GROWTH OF PRESCHOOL CHILDREN OF FIVE HEALTH CLASSES

MARY ELIZABETH EVANS, M.A.

LAWRENCE, KAN.

It has become a commonplace generalization among physicians, public health workers and others that the growth of children is retarded by pathologic conditions.¹ Some consider that retardation of growth is most marked as a result of severity of illness,² while others believe it to be most marked as a result of mild illnesses of long duration.³

Recourse to published studies shows that such generalizations are neither consistently nor extensively supported by experimental findings. Bowditch,⁴ using 1 girl as his subject, reported 3 instances in which a small loss in weight was a precursor of disease. Woodbury,⁵ using 57,977 children under 6 years of age, found stature and weight to be below average for those (203) with "rachitis" but not below average for those with a cardiac abnormality, diseased tonsils or adenoids. Turner, Lougee, Sarabia and Fuller,⁶ using some 120 school children, found that the children showing the poorest annual gains in weight were as a group "distinctly in-

ferior in respect to health behavior, amount of illness and number of physical defects when compared with the children who made the best growth." Palmer,⁷ employing 4,000 elementary school children of Hagerstown, Md., found no association between stature and weight on the one hand and absence from school for illness on the other. Hardy,⁸ from study of 600 children in attendance at the public schools of Joliet, Ill., did not find any relationship between number of illnesses in infancy and in childhood and stature at 20 years of age. Martens and Meredith,⁹ using 88 children between 5 and 6 years of age, reported no significant differences in rate of growth from fall to spring between children practically free from illness and children frequently absent from kindergarten for illness. Sontag and Lipford,¹⁰ using a group of 84 children, reported no association between aberrations in ossification of skeletal epiphyses and "acute or subacute" conditions of illness.

STATEMENT OF PROBLEM

None of the studies previously cited, with the exception of that of Woodbury,⁵ made any attempt to discover whether certain specific diseases or classes of disease are more closely associated with growth than others. From the clinical standpoint this is an important aspect of the general problem, and it is the aspect to which the present study is intended to contribute. Specifically, the aim of this paper is to add to the available information on the relation between history of illness and physical growth a study

This is the second of a series of studies on "Illness History and Physical Growth" made under the direction of Howard V. Meredith, Ph.D., Iowa Child Welfare Research Station, University of Iowa. The earlier study appeared in the American Journal of Diseases of Children (64:618-630, 1942).

1. (a) Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, ed. 9, New York, D. Appleton and Company, 1926, p. 11. (b) Jeans, P. C., and Stearns, G.: The Effect of Vitamin D on Linear Growth in Infancy: II. The Effect of Intakes Above 1,800 U. S. P. Units Daily, *J. Pediat.* **13**:730-740, 1938. (c) Sanders, B.: Environment and Growth, Baltimore, Warwick & York, Inc., 1934, p. 163.

2. MacCarthy, F. H.: The Healthy Child from Two to Seven, New York, The Macmillan Company, 1922, p. 167.

3. Jeans and Stearns,^{1b} pp. 733-734.

4. Bowditch, H. P.: The Relation Between Growth and Disease, *Tr. A. M. A.* **32**:371-377, 1881.

5. Woodbury, R. M.: Statures and Weights of Children Under Six Years of Age, Publication 87, United States Department of Labor, Children's Bureau, 1921.

6. Turner, C. E.; Lougee, W. W.; Sarabia, K., and Fuller, R. P.: Rate of Growth as a Health Index, *Research Quart.* (no. 3) **6**:29-40, 1935.

7. Palmer, C. E.: The Relation of Body Build to Sickness in Elementary School Children, *Am. J. Phys. Anthropol.* (supp.) **21**:7-8, 1936.

8. Hardy, M. C.: Frequent Illness in Childhood, Physical Growth and Final Size, *Am. J. Phys. Anthropol.* **23**:241-260, 1938.

9. Martens, E. J., and Meredith, H. V.: Illness History and Physical Growth: I. Correlation in Junior Primary Children Followed from Fall to Spring, *Am. J. Dis. Child.* **64**:618-630 (Oct.) 1942.

10. Sontag, L. W., and Lipford, J.: The Effect of Illness and Other Factors on the Appearance Pattern of Skeletal Epiphyses, *J. Pediat.* **23**:391-409, 1943.

of the growth in size of body of children having different specific diseases or having diseases classifiable in different relatively homogeneous groups.

EXPERIMENTAL MATERIAL

Subjects.—The subjects used for this investigation were 93 children of Iowa City, who were enrolled in the preschool laboratories of the Iowa Child Welfare Research Station during the period 1937 to 1942 inclusive. As will be explained later, no attempt was made to include every child enrolled during these years. The children were all white and were predominantly of northwest European ancestry. An analysis of the occupations of the fathers of the children showed that 64.5 per cent of the fathers followed professional occupations or had important managerial positions, 28 per cent were merchants or had minor managerial positions and the remaining 7.5 per cent were skilled laborers. The ages of the children at the initial, or fall, measurement varied from 2 years and 7 months to 5 years; at the second, or spring, measurement each child was 6 months older.

Data.—The anthropometric records employed were obtained routinely over the years encompassed by the study. Care was taken in the training of anthropometrists and in the maintenance of a rigorous technic. The procedures followed were those recently in use at the Iowa Child Welfare Research Station; they have been described in a publication by Knott.¹¹ All measurements were taken independently by two anthropometrists. From the fairly extensive series of measurements available the following were selected for use in the present investigation: stature; girth of arm; girth of leg; width of hip; circumference of chest; weight, and thickness of skin and subcutaneous tissue.

PROCEDURE

During the interim of six months between the fall and spring measurements daily records of absence for illness were obtained by a qualified nurse. She telephoned the homes of the children who were absent and kept a careful record of the reasons for absences. On the basis of these records the children were classified into five groups: group I, healthy children, who had been absent from preschool not more than a total of fourteen days during the six month period and who had had no single illness of more than two days' duration or classifiable as other than a minor cold or a minor digestive disturbance; group II, children who had been absent upwards of twenty-five days for minor infections of the respiratory tract; group III, children absent for prolonged illnesses, such as pneumonia and bronchitis; group IV, children absent for varying periods with either measles or chickenpox, and group V, children absent for at least twenty-five days because of both infections of the respiratory tract and digestive disorders. To be used as a subject, then, a child had to be classifiable either in group I (healthy children) or in one of the four groups that had illness. It follows that a child who had a moderately severe cough for two weeks in addition to measles would be excluded from the study as not clearly representative of either group IV (children with measles and chickenpox) or

group II (children with mild infections of the respiratory tract). Five of the 93 subjects had records which fulfilled one of the specifications listed for two consecutive six month periods. All of these records were used, so that a total of 98 records was available for the entire study.

Gains in the seven dimensions of the body over the six month period were obtained for each child and averages for each group computed. The averages of each of the groups subject to illness were compared with those of the healthy group. These comparisons were directed toward answering such questions as the following:

1. Do children who have frequent and severe colds during the winter months gain less in stature than children who are healthy?
2. Are the children who gain most in weight from fall to spring more healthy than those who gain least?
3. Does the girth of arm of children who have measles increase less rapidly than the girth of arm of healthy children?

OBSERVATIONS

Comparison of Group I and Group II

Group I was composed of 30 children who were absent from preschool for illness less than fifteen days during a six month period. As has been stated, no child was included in this group who had anything more than minor digestive disturbances or colds of one or two days' duration. Group II consisted of 34 children each of whom was absent for colds and/or coughs twenty-five days or more during a six month period. The distribution of the number of days absent for children in each of the two groups may be summarized as follows:

Days Absent from Preschool for Illness During a Fall to Spring Period of Six Months

	No. of Children	Mean	Minimum	Maximum
Group I.....	30	9.2	4	14
Group II.....	34	35.9	25	59

For each child in group I or group II increment values were derived, calculated from measurements of the body taken in the fall and again in the spring, after an interval of six months. The distributions of increments which resulted are epitomized in table 1.

TABLE 1.—*Semiannual (Fall to Spring) Gain and Loss by Children in Seven Physical Measurements*

	Group II (Children with Mild Illnesses of the Respiratory Tract)			Group I (Healthy Children)		
	Mean	Mini- mum	Maxi- mum	Mean	Mini- mum	Maxi- mum
Weight, lb.....	2.16	—1.58	5.70	2.55	—0.28	6.35
Stature, mm.....	36.1	23.0	46.0	38.0	28.0	53.0
Chest girth, mm.....	4.7	—20.0	23.0	8.2	—15.0	21.0
Hip width, mm.....	4.5	—2.0	9.0	4.7	—3.0	8.5
Arm girth, mm.....	1.9	—15.0	10.0	1.1	—8.0	8.0
Leg girth, mm.....	3.6	—9.0	12.0	4.0	—3.0	10.0
Thickness of skin and subcutaneous tissue, mm.....	—2.82	—16.0	6.0	—2.07	—10.0	4.5

11. Knott, V. B.: *Physical Measurement of Young Children: A Study of Anthropometric Reliabilities for Children Three to Six Years of Age, Studies in Child Welfare, Iowa City, University of Iowa, 1941, vol. 18, no. 3.*

The gains of group I (healthy children) in girth of chest, stature and weight were slightly greater than those of group II (children with mild illnesses of the respiratory tract). The two groups yielded almost identical means for girth of leg and width of hip, while the mean increase in girth of arm was slightly smaller for group I than for group II. The thickness of the subcutaneous fat (which here represents the sum of measurements of thickness taken over the abdomen, on the back of the arm and at the rear of the chest) is known to show a generally decreasing trend during the age period covered in the present study.¹² The means for loss in fatty tissue shown in the tabulation just given indicate that this loss was smaller for the healthy children (group I) than for those with mild illnesses of the respiratory tract (group II).

In order to determine whether or not the two groups were significantly different in any of the seven measures of rate of growth the *t* test was applied.¹³ It was found that in no dimension was the difference in gains for the two groups statistically significant (the values of *t* fell between 0.03 and 1.46).

Comparison of Group I and Group V

Group I (healthy children) has been previously described. Group V was composed of 14 children with mild illness of the respiratory and digestive tracts. Included here were such illnesses as "stomach upset and cold" and "cold, temperature and stomach disturbance." The distribution of number of days absent for these two groups may be summarized as follows:

Number of Days Absent from Preschool for Illness During a Fall to Spring Period of Six Months

	No. of Children	Mean	Minimum	Maximum
Group I.....	30	9.2	4	14
Group V.....	14	44.1	27	79

12. Meredith, H. V.: The Rhythm of Physical Growth: A Study of Eighteen Anthropometric Measurements on Iowa City White Males Ranging in Age Between Birth and Eighteen Years, Studies in Child Welfare, Iowa City, University of Iowa, 1935, vol. 11, no. 3. Boynton, B.: The Physical Growth of Girls: A Study of the Rhythm of Physical Growth from Anthropometric Measurements on Girls Between Birth and Eighteen Years, *ibid.*, 1936, vol. 12, no. 4.

13. Lindquist, E. F.: Statistical Analysis in Educational Research, Boston, Houghton Mifflin Company, 1940, pp. 51-54.

These comparisons parallel those of the previous section. The distributions which resulted are statistically reduced in table 2.

TABLE 2.—*Semiannual (Fall to Spring) Gain and Loss by Children in Seven Physical Measurements*

	Group V (Children with Mild Illnesses of the Respiratory and Digestive Tracts)			Group I (Healthy Children)		
	Mean	Mini- mum	Maxi- mum	Mean	Mini- mum	Maxi- mum
Weight, lb.....	2.08	-0.15	4.0	2.55	-0.28	6.35
Stature, mm.....	34.2	25.0	43.0	38.0	28.0	53.0
Chest girth, mm.....	5.4	-4.0	27.0	8.2	-15.0	21.0
Hip width, mm.....	4.1	1.0	8.0	4.7	-3.0	8.5
Arm girth, mm.....	4.5	-5.0	12.0	1.1	-8.0	8.0
Leg girth, mm.....	4.7	-5.0	11.0	4.0	-3.0	10.0
Thickness of skin and subcutaneous tissue, mm.....	-2.60	-8.0	3.0	-2.07	-10.0	4.5

Compared with the mean gains for group I, the mean gains for group V tended to be larger for girth of arm and of leg and smaller for weight, stature, girth of chest, and width of hip. Group V lost more in thickness of skin and of subcutaneous tissue than did group I.

As in the case of the previous comparison, the Fisher *t* test was employed. With one exception the *t* values were not statistically significant at either the 1 per cent or the 5 per cent level of confidence. For girth of arm, $t = 2.34$; this, however, will be seen to imply that the group having mild illnesses of the respiratory and digestive tracts showed a greater gain in girth of arm over the six month period than did the healthy group.

Comparison of Group I and Group IV

Group I (healthy children) has been previously described. Group IV was composed of 11 children who during the half-year period had measles or chickenpox, uncomplicated by other significant illness. Of these 11, 7 had chickenpox and 4 had measles. The following is a summary of the number of days absent from preschool:

Days Absent from Preschool for Illness During a Fall to Spring Period of Six Months

	No. of Children	Mean	Minimum	Maximum
Group I.....	30	9.2	4	14
Group IV.....	11	32.0	19	57

Statistical reduction of the distributions of increments for the two groups are presented in table 3.

TABLE 3.—Semiannual (Fall to Spring) Gain and Loss of Children in Seven Physical Measurements

	Group IV (Children with Measles or Chickenpox)			Group I (Healthy Children)		
	Mean	Mini- mum	Maxi- mum	Mean	Mini- mum	Maxi- mum
Weight, lb.....	2.44	0.3	6.4	2.55	-0.28	6.35
Stature, mm.....	36.1	25.0	48.0	38.0	28.0	53.0
Chest girth, mm.....	5.8	-1.0	24.0	8.2	-15.0	21.0
Hip width, mm.....	5.6	1.0	10.0	4.7	-3.0	8.5
Arm girth, mm.....	3.1	-4.5	15.0	1.1	-8.0	8.0
Leg girth, mm.....	5.9	-2.0	13.0	4.0	-3.0	10.0
Thickness of skin and subcutaneous tissue, mm.....	-0.35	-8.0	1.0	-2.07	-10.0	4.5

The means here do not indicate any definite trend. It will be seen that group I showed a more rapid rate of increase in circumference of chest, stature and weight, while the "measles-chickenpox" group made slightly greater gains in girth of arm, girth of leg, and width of hip. The healthy children lost more subcutaneous fat than did those who had measles or chickenpox.

Again the Fisher *t* test was used to determine whether or not the two groups differed significantly in amounts of growth. In no instance did *t* exceed 1.70. It follows that there is no basis for rejecting the hypothesis that both groups represent the same increment populations.

Comparison of Group I and Group III

Group I (healthy children) has already been described. Group III was comprised of 9 children whose health histories showed severe or prolonged mumps, infection of tonsils, influenza, bronchitis or pneumonia. The following tabulation summarizes the records of absence:

Days Absent from Preschool for Illness During a Fall to Spring Period of Six Months

	No. of Children	Mean	Minimum	Maximum
Group I.....	30	9.2	4	14
Group III.....	9	58.3	12	145

A reduction of the seven increment distributions for each group is shown in table 4.

TABLE 4.—Semiannual (Fall to Spring) Gain and Loss of Children in Seven Physical Measurements

	Group III (Children with Prolonged Illnesses)			Group I (Healthy Children)		
	Mean	Mini- mum	Maxi- mum	Mean	Mini- mum	Maxi- mum
Weight, lb.....	2.60	0.9	4.3	2.55	-0.28	6.35
Stature, mm.....	37.3	29.0	43.0	38.0	28.0	53.0
Chest girth, mm.....	7.1	-1.0	17.0	8.2	-15.0	21.0
Hip width, mm.....	5.6	3.0	7.0	4.7	-3.0	8.5
Arm girth, mm.....	1.8	-4.0	10.0	1.1	-8.0	8.0
Leg girth, mm.....	7.6	4.0	13.0	4.0	-3.0	10.0
Thickness of skin and subcutaneous tissue, mm.....	-2.3	-7.0	6.0	-2.07	-10.0	4.5

Again, no systematic difference is obtained between the means. Group I lost less in thickness of subcutaneous tissue, gained more in stature and girth of chest and gained less in girth of arm and of leg than did group III.

In an attempt to discover whether the gains of the two groups were significantly different, the *t* test was used. At the 1 per cent level of confidence there is no evidence that the two groups differed in rate of growth. For one item only, gain in girth of leg, did the two groups differ significantly at the 5 per cent level of confidence. For these particular samples it will be noted that the gains in girth of leg were higher for the group with prolonged illnesses than for the healthy group.

ANALYSIS OF FOUR CASES FROM GROUP III.

CASE 1.—K. C., a girl whose age at the initial fall measurement was 3 years and 5 months, was absent for illness a total of ninety-two days during the ensuing six month period. The causes of her absences were as follows: inflammation of the throat, cold, nasal discharge and infection of the tonsils (causing an absence of six weeks), removal of tonsils and adenoids. The following tabulation compares her increments with the mean increments of the "healthy" group:

Comparison of Gains of K. C. with Means of Group I (Healthy Children)

	K. C.	Group I
Weight, lb.....	4.3	2.55
Stature, mm.....	43.0	38.0
Chest girth, mm.....	9.0	8.2
Hip width, mm.....	7.0	4.7
Arm girth, mm.....	6.0	1.1
Leg girth, mm.....	10.0	4.0
Thickness of skin and subcutaneous tissue, mm.....	-1.0	-2.07

In every body dimension studied K. C. gained more than the mean gain of group I.

CASE 2.—M. S., a boy 4 years and 6 months old at the time of the initial fall measurement, was absent for illness a total of fifty-three days during the succeeding six months. Items included in his history of illness were: hoarseness; cold, and cold, temperature and influenza (causing an absence of six weeks). The following tabulation compares his increments in seven aspects of body size with those of group I:

Comparison of Gains of M. S. with Means of Group I

	M. S.	Group I
Weight, lb.....	3.1	2.55
Stature, mm.....	29.0	38.0
Chest girth, mm.....	17.0	8.2
Hip width, mm.....	6.0	4.7
Arm girth, mm.....	10.0	1.1
Leg girth, mm.....	4.0	4.0
Thickness of skin and subcutaneous tissue, mm.....	0.0	-2.07

M. S.'s increments will be seen to exceed those of group I except for girth of leg and for stature.

CASE 3.—P. C., a girl whose age at the initial fall measurement was 3 years and 9 months, was absent for illness a total of fifty-seven days during the following

six month period. Her illnesses were as follows: cold, cold, influenza and pneumonia (causing an absence of six weeks), and minor cold. A comparison of her body growth with that for group I follows:

Comparison of Gains of P. C. with Means of Group I

	P. C.	Group I
Weight, lb.....	1.6	2.55
Stature, mm.....	38.0	38.0
Chest girth, mm.....	1.0	8.2
Hip width, mm.....	6.0	4.7
Arm girth, mm.....	2.0	1.1
Leg girth, mm.....	8.0	4.0
Thickness of skin and subcutaneous tissue, mm.....	-3.0	-2.07

It will be seen that P. C. gained more than did group I in girth of arm, girth of leg and width of hips. She gained identically with group I in stature. In weight and girth of chest P. C.'s gains were less than the mean gains of group I.

CASE 4.—L. M., a boy whose age at the initial fall measurement was 3 years and 9 months, was absent for illness a total of one hundred and forty-five days during the ensuing six months. His absences from preschool were recorded as follows: minor cold and pneumonia due to streptococcal infection (white cell count low; this notation covered an absence of four and one-half months). This child, then, was below par physically for over two thirds of the period covered. His gains as compared with the mean gains of the healthy group are presented in the following tabulation:

Comparison of Gains of L. M. with Means of Group I

	L. M.	Group I
Weight, lb.....	2.9	2.55
Stature, mm.....	36.0	38.0
Chest girth, mm.....	2.0	8.2
Hip width, mm.....	5.0	4.7
Arm girth, mm.....	1.0	1.1
Leg girth, mm.....	9.0	4.0
Thickness of skin and subcutaneous tissue, mm.....	-1.0	-2.07

L. M.'s gains will be seen practically to equal the mean gains for group I in stature, girth of arm and width of hip. In weight and in girth of leg L. M.'s gains were the higher, while in chest girth the mean of group I was the higher.

SUMMARY

The present investigation is intended to contribute to a solution of the general problem of the relationship between illness and physical growth. Specifically, its purpose is to compare the growth over a six month period of children classified in five groups on the basis of records of their illnesses.

The subjects were 93 children between the ages of 2½ and 5 years who were enrolled in the preschool laboratories of the University of Iowa. The histories of their illnesses were amassed through the medium of daily records compiled by an experienced preschool nurse. An anthropometric examination of each child was made

in the fall and another after an interval of six months. The children were grouped into five classes according to their records of illness: group I, healthy children; group II, children with mild illnesses of the respiratory tract; group III, children with prolonged illness; group IV, children with measles or chickenpox, and group V, children with infections of both the respiratory and the digestive tracts. Analyses were made for gain or loss in seven anthropometric measurements: stature, weight, girth of arm, girth of leg, girth of chest, width of hip and thickness of skin and of subcutaneous tissue.

The physical growth of the healthy group was aligned successively with that of each of the four groups having illness. By means of the *t* test it was ascertained that in twenty-eight comparisons only two were statistically significant. The gains in girth of arm for group I (healthy children) and for group V (children with mild illnesses of the respiratory and digestive tracts) were significantly different at the 1 per cent level of confidence, and the gains in girth of leg for group I (healthy children) and for group III (children with prolonged illness) were significantly different at the 5 per cent level of confidence. In both these instances the gains were greater for the groups having illness than for the healthy group.

Individual study was made of 4 subjects absent for illness upward of fifty days each. When the gains of these children were compared with the mean gains of the healthy group no consistent or marked differences were found.

It may be said, then, that the children who were absent from preschool because of illness gained approximately the same amount as did the children who were almost entirely free from illness.

In interpreting these results the fact that the children came from homes of relatively high socioeconomic status must be borne in mind. These children, presumably, received better than average care of their health at all times and were given special attention during illnesses. These children, too, were kept at home until such lingering manifestations of illness as fatigue and listlessness had disappeared. It is possible that a study done on children from homes of lower socioeconomic levels might not yield the same results as the present investigation.

1343 Tennessee Street.

Case Reports

PYGOPAGUS TWINS

REPORT OF DISSECTION OF THE THORAX, ABDOMEN AND PELVIS

HELEN DAWSON, Ph.D.

IOWA CITY

The S. twins were admitted to Children's Hospital, State University of Iowa, Iowa City, on Aug. 14, 1942, at the age of 3 weeks. They died Dec. 7, 1942 and at that time were brought to the department of anatomy for dissection. This paper is a report of the gross observations.

HISTORY

Janet and Judith S., Siamese twin girls, were born July 21, 1942 at Dubuque, Iowa. The father and mother were of white American stock, aged 26 and 21 years respectively. These were their first children. There was a history of twins on both the maternal and the paternal side, but no other Siamese twins were known in the family.

The parents of the twins lived on a farm near New Vienna, Iowa, with the father's parents. The family had a moderately low income.

The twins were full term babies. Labor lasted nineteen hours, from 4:30 a. m. until 11:30 p. m. Capt. C. B. Hall, the physician who delivered the twins, sent the following report concerning the placenta:

"The placenta was expressed easily after 1 ampule of pitocin had been given intramuscularly, with minimal loss of blood. The placenta was single, with a single chorionic membrane enclosing both babies. The amniotic membrane was closely fused to the chorion, as though each baby had a separate amnion. The cords arose 7 cm. apart on the fetal surface of the placenta. . . . The placenta itself was of average thickness, ovoid and slightly larger than normal in over-all measurement."

It is doubtful that each baby had a separate amnion; it is more likely that there was a pouched condition, which might have been mistaken for separate amnions.

The weight of the twins at birth was 9 pounds 10 ounces (4,366 Gm.). The right twin (Janet) was a "blue baby." The point of union between the two was in the region of the buttocks (fig. 1).

At the time they were admitted to the hospital the twins appeared dehydrated, and their weight was subnormal (4,300 Gm.). They had spina bifida and a common meningocele (fig. 2). On their admission to the hospital both infants showed slight hydrocephalus. There was an apparent defect in the ribs on the right side of the left twin (Judith). The anal opening was single and in the line of union of the two infants, toward the posterior surface. The external genitalia were common to the twins. There was a single vestibule which presented four separate, small openings for the urethras and the vaginas. The extremities of the left twin appeared normal. While the upper extremities of the right twin were normal, the lower

extremities were poorly developed, and the right leg had not rotated completely. Except for the defective thorax the left twin appeared to be the better formed and sturdier of the two.

Roentgenograms were made of the children, and the report was as follows: "Roentgen studies of the entire bodies of the conjoined twins show them to be united at the sacral areas. Both appear to have complete innominate bones, but the centers of ossification for the sacra appear continuous, and the sacra appear to be joined. One twin demonstrates a spina bifida vara, and films of both skulls show a condition described as *Lückenschädel*. Except for the fusion of the sacra the skeletons appear complete and separate; both show anomalies of the ribs in the midthoracic regions."

The twins were first brought to my attention on Aug. 26, 1942, when a number of anthropologic measurements and observations were made. Measurements were taken again on Sept. 10, 1942. Attempts were made at different times to obtain prints of the fingers and hands for study.

The immediate cause of death was considered to be "respiratory paralysis" due to the Arnold-Chiari syndrome. Judith, the left twin, was pronounced dead at 8:15 a. m. on Dec. 7, 1942, and Janet, the right twin, at 8:50 a. m.

Necropsy.—After their death complete dissections were made of the thorax, the abdomen and the pelvis of each twin. The brains and the lower segments of the spinal cord were removed and preserved for future study. Although a complete dissection of the lower extremities would have been desirable, time was limited, and further work was impossible. Histologic sections were made of various organs and structures; a report will be made on them in a separate paper.

RIGHT TWIN (JANET)

The right twin seemed to be the more poorly developed. She was thinner than her twin and the lower extremities were defective. She had marked hydrocephalus, and the head was misshapen and skewed.

An incision was made along the entire anterior surface of the body, from the suprasternal notch to the pubis. Incisions were then made from the suprasternal notch laterally to the acromions. Skin and superficial fascia were reflected laterally, and the sternum and a portion of the ribs were removed.

Thorax.—When the thorax was first opened the organs appeared normal (fig. 3). The heart was normal in size and placed in the midline with the apex toward the left. The lungs appeared normal.

Lungs: On closer inspection the right lung showed the usual three lobes but was considerably larger than the left lung. Nothing unusual was noticed about the arrangement of the structures entering the root of the right lung. The left lung, while noticeably smaller

From the Department of Anatomy, State University of Iowa.

than the right, showed normal configuration. It had two well defined lobes and a distinct cardiac notch. The posterior surfaces of both lungs showed marked ribbing, the soft tissue having been compressed by the defective thoracic wall. Most of the inferior lobe of the right lung and the posterior quarter of the left lung were consolidated, hard and dark red.

Thymus: The thymus was relatively large. It covered and hid the upper half of the heart and was closely applied to the pericardial sac laterally, separating it from the lungs on both sides. The thymus had a well developed medial lobe, which projected upward into

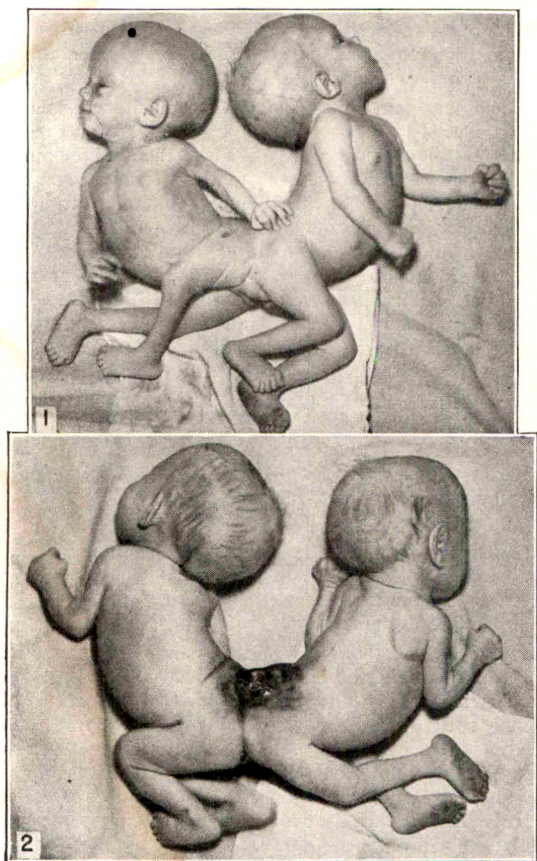
extend horizontally, with the pyloric portion higher than was expected. The coiled intestines were difficult to differentiate, the small intestine being relatively large. It was difficult to identify the cecum or the ascending or transverse colon.

Liver: The liver appeared from the front to be of normal size, but on closer inspection the posterior-inferior margin of the right lobe was found to extend down the back wall of the abdomen to approximately 1.5 cm. below a horizontal plane on a level with the umbilicus. The falciform ligament was attached to the diaphragm 7 mm. to the right of the tip of the xiphoid process. The round ligament was large, but the lumen was no longer patent.

Gallbladder: The gallbladder appeared normal in size, position and color (fig. 4), as did the cystic duct.

Spleen and Pancreas: The spleen and the pancreas showed nothing unusual enough to warrant description.

Stomach and Intestines: The only features concerning the alimentary tract which are of interest were the variations in position of certain segments due to incomplete rotation of the intestines; the previously mentioned relatively large size of the small intestine;



Figs. 1 and 2.—1, anterior view of twins. 2, posterior view of twins, showing meningocele.

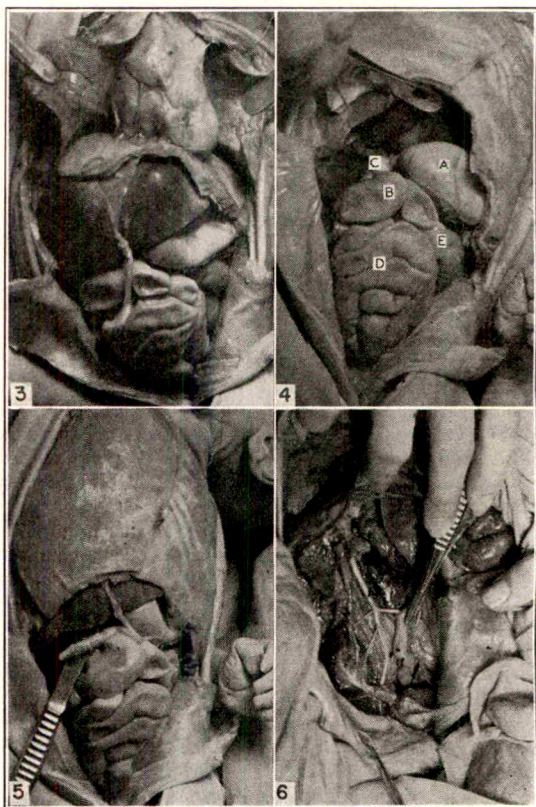
the neck, extending approximately 2 mm. above the suprasternal notch.

Heart: There was nothing unusual about the pericardium or the heart (fig. 3). The ductus arteriosus was patent, and the foramen ovale was partially open. The vessels arising from and entering the heart were normal in number and position.

Blood Vessels: The vessels supplying the organs of the thoracic area were similar to the normal organs described in Gray's "Anatomy"; nothing unusual enough to warrant description was encountered.

Nerves: The course and relationships of the vagus and phrenic nerves were normal.

Abdomen.—When the abdomen was opened, the liver, stomach and intestines lay exposed (fig. 4). The greater omentum was not visible. The liver appeared normal in size and position. The small portion of the stomach which could be seen seemed to be placed a little too far to the left, and the long axis appeared to



Figs. 3 to 6.—3, thoracic and pelvic viscera of the right twin. Note the large thymus, which partially hides the heart. 4, abdominal viscera of the right twin: A, stomach; B, cecum; C, ileum; D, small intestines; E, transverse colon. 5, photograph showing position of the cecum and the appendix in the right twin. 6, the mesenteries for the alimentary tract of the right twin have been cut and the intestines removed from the abdominal cavity in order to expose the urinary organs, their blood supply and the adrenal glands. Note the position and the rotation of the right kidney. The three divisions of the ureter are clearly visible.

four points of intussusception, and the presence of a mesentery in certain areas.

Because of certain peculiarities in the position of the large intestine and the relatively large size of the small intestine it will be necessary to refer to figures 4 and 5 for orientation. The stomach was displaced slightly to the left, and the long axis was horizontal. The pyloric portion was directed posteriorly and lay to the left of the gallbladder. The small intestine (ileum), which was relatively large, the cecum and a small segment of the transverse and the descending colon (fig. 4) were the only portions of the large intestine visible when the abdomen was opened. A portion of the ileum, approximately the lower one third, occupied the right lower quadrant, taking the position normally occupied by the cecum and the ascending colon. In figure 4 the terminal part of the ileum can be seen in its relationship with the cecum on the right and the pyloric portion of the stomach on the left. The duodenum lay behind the last portion of the ileum (fig. 4). The cecum, instead of being in the lower right quadrant as would be expected, was pressed closely against the under surface of the right lobe of the liver. The appendix measured 3 cm. and was located between the cecum and the liver (fig. 5). The ascending colon zigzagged transversely from right to left several times before it was intussuscepted into the transverse colon, and it carried with it the greater omentum and the mesentery of the ascending colon. The course and relationship of the descending and the sigmoid colon and of the rectum were normal. Both the descending portion of the colon and the rectum were smaller in diameter than the rest of the intestinal tract. In addition to the intussusception of the ascending colon into the transverse colon, there were three areas of intussusception in the small intestine. Probably these four areas of intussusception represent agonal changes at the time of death and were not a contributing factor in the death of this twin. The positions of the various segments of the intestine were indicative of its incomplete rotation. The possibility of arrested development of the large intestine is further substantiated by the presence of a mesentery throughout the entire length of the large intestine. The shortest mesentery was found for the upper part of the descending colon.

Adrenal Glands: Both the right and the left adrenal gland in the right twin were large (fig. 6). The left adrenal gland, which was the smaller of the two, was placed directly above and in close contact with the upper pole of the left kidney. The right adrenal gland was large and was pressed between the posterior surface of the right lobe of the liver and the diaphragm. Its lower border was 1.3 cm. above the superior pole of the right kidney (fig. 6).

Kidneys: The right kidney was larger than the left and placed much lower in the abdomen. The shape was distorted, as is shown in figure 6. The right kidney was rotated on its long axis so that the pelvis of the ureter was directed anteriorly and laterally. The lower pole of this kidney was on a plane 6 mm. below the bifurcation of the abdominal aorta. The upper pole was opposite the origin of the inferior mesenteric artery. Three arteries entered the right kidney; their origin and distribution will be discussed later. The venous return was by way of a main renal vein from the hilus and two small tributaries from the superior pole of the kidney. The left kidney appeared normal in both size and position. The lower pole of the left kidney was opposite a point 3 mm. below the origin of the inferior mesenteric artery, and the upper pole was 5 mm. below the origin of the superior mesenteric artery. There was a single artery which entered at the hilus of the kidney. The renal vein was large.

Ureters: The ureter on the right showed a peculiarity in its mode of origin. Instead of starting as a single pelvis from the hilus of the kidney, it began as three separate small pelvises (fig. 6), which joined to form a single ureter. The ureter on the left side was normal. Both ureters were normal in size and in their relationships and emptied into the bladder in the usual manner.

Blood Vessels: In general the blood vessels in the abdominal region showed no unusual variations. Mention should be made, however, of those supplying the right kidney. Three separate arteries, all derived from the aorta, supplied this organ (fig. 6). The highest artery was intermediate in size. It arose from the right side of the aorta opposite the origin of the inferior mesenteric artery. It extended laterally to the right and slightly downward to enter the superior pole of the kidney. The middle and largest of the three arteries arose 7 mm. below the inferior mesenteric artery and extended laterally to the right and downward to enter the hilus of the kidney. (Because of the lateral rotation of the kidney on its long axis, the artery crossed the kidney to enter on its anterior surface.) The third and smallest of the right renal arteries took its origin 1.3 cm. below the inferior mesenteric artery. It crossed behind the second renal artery to enter the kidney on its posterior surface at a point opposite the hilus. The left renal artery took its origin from the descending aorta 2 mm. above the inferior mesenteric artery and entered the kidney at the hilus.

The venous drainage from the right kidney was by one main vein from the hilus and two small tributaries from the superior pole of the kidney. These vessels drained into the inferior vena cava. The large left renal vein left the hilus of the kidney, crossed posterior to the aorta and entered the inferior vena cava 6 mm. above its origin.

Nerves: The vagus and splanchnic nerves entered the abdominal region in the usual manner. No attempt was made to work out the details of the various plexuses.

Pelvis.—Bladder: The middle umbilical ligament and fold were prominent. Where the middle umbilical ligament left the vertex of the bladder, it presented a hard pyramidal-shaped portion, the base of which rested on the bladder and the apex of which projected upward (fig. 6). There was a well developed lateral umbilical ligament on the right side, but none was found on the left side. The bladder was of moderate size and conformed to the usual descriptions of the bladders of infants. It was apparently occluded, since it could not be decompressed. On being opened it was found to contain air and a clear, almost colorless fluid. On probing, an obstruction was found at the neck of the vesicle. Since the bladder was not abnormally distended, the obstruction was probably produced by strong contraction of the sphincter vesicae shortly before or at the time of death. As might be expected from the fusion of the twins in the pelvic region and the close relationship of the urethras and genital organs of the right and left twins, the bladders in their lower parts and the urethras were closely bound together by dense, fibrous connective tissue. The urethra of the right twin was patent but greatly constricted at the internal orifice. It began at the apex of the trigone vesicae; the external orifice may be seen as the upper left opening in figure 18.

Genital Organs: The reflection of the peritoneum was the same as is usually described except for one or two variations, which will be mentioned briefly during the description. The peritoneum formed a short mesovarium as it was reflected on the ovary; then it extended back to the posterolateral wall on the right side

fastening the organs snugly to the posterior abdominal wall. On the right side the ovary lay almost vertically; the superior pole (the one nearest the fimbriated extremity of the uterine tube) was directed slightly laterally. The tube lay lateral to the ovary, and the fimbriated extremity was folded back on itself. The ureter was directly posterior and closely applied to the tube. The superior pole of the right ovary overlapped the inferior pole of the right kidney approximately 2 mm. The right ovary was narrow, thin and elongated and was oddly club shaped. It was 2.6 cm. in length, while its upper and widest part measured 5 mm. It then tapered to only 3 mm. at a point 3 mm. from its distal tip. The left ovary was the usual oval shape, 1.5 cm. long, 8 mm. wide and approximately 3 mm. thick. On the left side the lower pole of the kidney was approximately 2.5 cm. above the upper pole of the ovary.

On a level with the left ureter the peritoneum left the posterolateral wall to reflect and form the mesentery for the lower part of the colon and the rectum. What appeared to be a poorly developed broad ligament containing ovaries and uterine tubes was observed. The organs on the left side lay at a lower level (distally) than the ones on the right side. The difference between the superior poles of the ovaries on the right and left sides was approximately 1 cm.

The uterus was deep in the pelvic cavity between the bladder and the rectum. The long axis of the uterus was in a straight line with the long axis of the vagina. The uterus was flattened anteroposteriorly and presented a concave surface posteriorly both from side to side and from apex to base. It was not truly piriform when viewed from the front, but was shaped more like the sole of a slipper. The left uterine tube entered the upper left margin of the uterus; on the right side the tube entered slightly lower than on the left side. The vaginal portion of the uterus projected into the vagina about 3 mm. The lips of the uterus were smoothly rounded and seemed to be of about the same size.

The vagina extended from the uterus to the vestibule. In its entire extent it was closely bound to the vagina of the left twin. At the vestibule the medial walls of the two vaginas were of the same thickness as the septums separating the two orifices.

Blood Vessels: Those blood vessels which were dissected in detail conformed for the most part to the descriptions in Gray's "Anatomy," only minor variations being encountered. The only vascular connection found between the twins was the anastomosis between the middle sacral arteries. These arteries were unusually large (figs. 19 and 20).

Nerves: No attempt was made to work out the details of the nerves in this region.

LEFT TWIN (JUDITH)

At the time of the dissection the left twin seemed to be fairly well nourished. She showed a defect in the region of the thorax on the right side, where the bony ribs were missing. Like the right twin, she had extreme hydrocephalus and a badly misshapen head.

The body was opened in the same manner as was reported for the right twin.

Thorax.—When the thorax was opened the organs were found to be abnormal in size and in position. Part of the disarrangement was due to the displacement produced by the extremely large size of the liver and the resulting encroachment of this organ on the thoracic area. The large size of the right lung is evident from figure 7. It was wider from side to side

than from apex to base, and it extended beyond the midsagittal line about 1 cm. onto the left side of the thorax. The heart was also displaced toward the left; the entire organ lay to the left of the midsagittal line. The apex of the heart was directed to the left. The left lung was small, atelectatic and deep red. It could scarcely be seen from the front. Figure 8, which is a lateral view, shows the left lung in its relation to other thoracic organs. The thymus was large. The right edge of the thymus came to the midsagittal line; the rest of the organ was displaced to the left and covered the upper half of the heart (figs. 7 and 8).

Lungs: When the lungs were examined more closely, both showed the normal number of lobes, but the car-

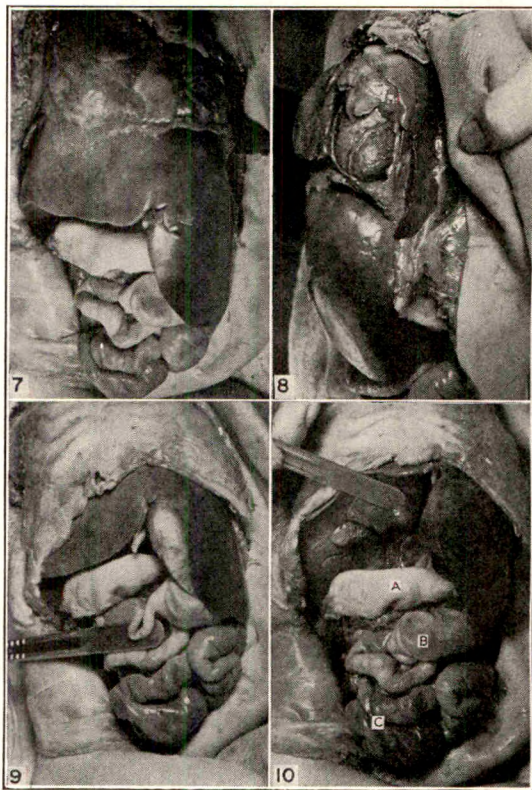


Fig. 7 to 10.—7, thoracic and abdominal viscera of the left twin. Note the extremely large liver. The large right lung, which is rotated, extends beyond the midline. The heart is crowded to the left. The left lung is small, and only a small portion can be seen. 8, photograph of viscera of the left twin taken from the left side. Observe the compressed atelectatic left lung. The heart is large and partially covered by the large thymus gland. The extremely large left lobe of the liver almost completely hides the intestines. 9, photograph of the left twin showing the position of the cecum and the appendix. 10, abdominal viscera of the left twin: A, stomach; B, cecum; C, small intestines.

diac notch on the left lung was indistinct. The right lung was found to be rotated so that the fissures, instead of being in a horizontal plane, were turned until they were directed nearly vertically. Because of the twisting and distortion of the lung, the tissue of the right lung overlay the vessels, the right atrium and most of the right ventricle of the heart. The lateral edge of the right lung showed an area of consolidation and was dark red. There was a depression on the

superior surface (apex) due to a thoracic deformity. The left lung was small, dark red and atelectatic. Only the lower tip of this lung could be seen from the front (fig. 7). However, the lung extended down and behind the heart and was almost hidden by it. A lateral view showed it to be long, thin and crowded laterally by the pressure of the other organs. The atelectasis is probably due to mechanical pressure; examination of the trachea and the bronchus showed no evidence of any obstruction in the bronchial tree. The posterior surfaces of both lungs showed slight "ribbing," but it was not as marked as in the right twin.

Thymus: The thymus was large and lay completely to the left of the midsagittal plane of the thorax. It covered the upper half of the heart. Two "tongues" of thymic tissue extended into the neck. The right tongue projected 1 cm. above the suprasternal notch; the left, which was longer, extended 1.5 cm. upward.

Heart: This organ was of good size but was crowded toward the left and was rotated so that the superior vena cava was anterior. Both atria and both auricles were large. The surface of the ventricles was rough and shrunken looking, but there were no adhesions to the pericardium. The ductus arteriosus was patent, and the foramen ovale was not closed. The pulmonary artery lay to the left and on a plane posterior to the superior vena cava. The aorta lay to the left and behind the superior vena cava.

Blood Vessels and Nerves: The peculiarities which were encountered in the blood vessels and the nerves were due to abnormalities in the position of the organs supplied by these structures rather than to anomalies of the vessels or nerves themselves.

Abdomen.—The most startling thing about the abdominal organs at the first glimpse was the extremely large liver (fig. 7), which filled the entire upper half of the abdominal cavity. Superiorly it extended upward as high as the nipple line, causing compression and disarrangement of the thoracic structures. The left lobe was very large and extended downward to the level of the umbilicus. The falciform ligament lay to the left of the midsagittal line. The round ligament was prominent but was occluded. The stomach showed below the right lobe of the liver and lay in a horizontal plane. The omentum was gathered tightly against the greater curvature of the stomach and did not cover the intestines as the normal omentum does. The arrangement of the large intestine was confusing at first glance. The cecum was on the left (fig. 9) and at first was thought to represent a partial situs inversus, but closer examination showed that here again the intestine had failed to rotate completely. The difference in size between the large and small intestines was apparent, and less difficulty was encountered in differentiating them than in the case of the right twin. The orientation of the rest of the intestines can best be accomplished by referring to figure 10.

Liver: The liver was prominent. The left lobe particularly was extremely large and extended to the left side of the abdominal wall. The lower extremity of the left lobe, which extended downward to the level of the umbilicus, crowded the intestines toward the midline, distorting their arrangement. Because of the large size of the liver and the changed relationships of the abdominal structures, the normally well defined impressions on the inferior surface of the liver were faint and poorly marked. There were, however, well developed caudate and quadrate lobes. On the posterolateral surface of the right lobe there was a prominent mass of hepatic tissue which projected as a "tongue" into the fossa (caused by a skeletal defect) on the

posterolateral wall of the abdomen. This tongue of hepatic tissue was hard and dark red, which indicated an area of marked congestion.

Gallbladder: The gallbladder was of normal size, color and position. It was moderately filled with bile. The cystic duct and the common duct appeared to be normal.

Spleen and Pancreas: The spleen lay directly in the midline plane of the body, crowded between the right and left lobes of the liver. Its long axis was directed almost vertically, the lower pole of the spleen being slightly to the left of the upper pole. In this position it was forced behind the esophagus, which almost completely hid it. Except for this disarrangement in its position the spleen appeared normal.

There was nothing about the pancreas so significantly different as to warrant description.

Stomach and Intestines: The stomach was large; approximately half of it protruded below the margin of the liver. Its long axis was directed in a horizontal plane. The pyloric portions (the antrum and the pylorus) were pressed against the gallbladder, and the upper surface was stained with bile. On the right side of the cardiac portion of the stomach was a large eroded area, showing the effect of postmortem autolysis; this area was pressed firmly against the neighboring liver.

No attempt will be made to describe in detail the intricate arrangement of the intestines. The small intestine filled the middle and the lower part of the right half of the abdomen. The duodenum lay below the posterior half of the right lobe of the liver and was entirely hidden by folds of the ileum and of the ascending and the transverse colon. The jejunum was also deeply located in the upper right quadrant of the abdomen. The greater part of the coils of the small intestine was disposed in the middle and lower parts of the abdomen (fig. 10). The terminal portion of the small intestine appeared just below the extreme right tip of the stomach, extended downward and curved left to enter the posteromedial surface of the cecum. About midway along the small intestine there was a double intussusception (fig. 11). When this was examined, it appeared to be due to postmortem changes, since there was no evidence of gangrene or other indication that it might have been the primary cause of death in this twin.

The cecum lay to the left of the midsagittal plane and was partially hidden by the left lobe of the liver. The appendix, which measured 3.1 cm., came off the medial side of the cecum; the terminal half and the tip of the appendix were folded back on the first half and directed forward and medially. The ascending colon lay first along the left abdominal wall for a short distance and then extended transversely to the right. The transverse segment of the colon began at the right side of the abdomen, where the ascending colon made a U turn. The terminal portion of the transverse colon lay behind the descending colon and below the stomach. The descending colon lay along the back of the abdominal cavity approximately 1.5 cm. lateral to the midline. It extended downward along the lateral margin of the left kidney; a short distance distal to the lower pole of the kidney the colon turned medially to enter the sigmoid portion. The sigmoid colon and the rectum showed nothing unusual in position or relationships. There was a well developed mesentery for the entire intestinal tract. The mesentery for the cecum was particularly long and well developed (fig. 12). The shortest mesentery was in the region of the descending colon. Again, what appeared at first glance to be an example of partial situs

inversus turned out to be arrested development with incomplete rotation of the intestine.

Adrenal Glands: The adrenal glands were both large (fig. 13). The left was the smaller of the two. It was roughly triangular in shape and lay directly above the left kidney and at a somewhat lower level than the right adrenal gland. The right adrenal gland was a large organ somewhat semilunar in shape. Its upper half was in contact with the diaphragm posteriorly and covered a relatively large defect in the thoracic cage and the diaphragm to the right of the vertebral column. There was a prominent projection of the adrenal tissue on the posterior surface of the upper half of the gland that fit and filled the fossa produced by the bony de-



Figs. 11 to 14.—11, double intussusception of the large intestine in the left twin. 12, abdominal viscera of the left twin. Notice the well developed mesentery extending across to the cecum. 13, the mesenteries of the left twin have been cut and the intestines pulled to one side in order to expose the posterior abdominal wall. Note the distended left ureter. There was no kidney on the right side. The peculiarly shaped structure (A) was found to be an ovary and a uterine tube. 14, abdominal viscera of the left twin. The right adrenal gland has been reflected toward the midline. The probe is lifting the sympathetic nerve trunk.

formity and the diaphragmatic deficiency. The sympathetic chain of fibers entered the abdomen through the hiatus in the diaphragm behind the right adrenal gland (fig. 14).

Kidneys: There was only a left kidney in the left twin, and it was large and placed relatively low. The inferior pole was in a plane on a level with the bifurcation in the abdominal aorta. The left ureter was irregular in size throughout its course. At the pelvis it lay deep to the arteries and the vein, being directly in relation with the artery. As it left the kidney it was about the same size as the ureters in the right

twin. At a distance of 4 cm. from the hilus of the kidney the diameter of the ureter was exactly tripled; then it again became somewhat smaller. The wall of the dilated portion was very thin. The cause of the dilatation was not determined, since the opening into the bladder seemed patent. On the right side there was no kidney or evidence of any remnant of one. On the posterior abdominal wall on the right side there was an odd structure which measured 3.1 cm. in length. This structure lay retroperitoneally, and its long axis was directed vertically (fig. 13). Histologic examination showed it to be the ovary and the uterine tube.

Blood Vessels: The abdominal aorta entered the abdominal cavity through the aortic hiatus. It extended downward behind the right lobe of the liver, lying to the right of the inferior vena cava. Within a relatively short distance it crossed deep to the vena cava and assumed its normal relationship to this vessel. It terminated at the level of the fifth lumbar vertebra, in the two common iliac arteries.

Only two variations in the blood vessels of the abdominal region warrant discussion. The left gastric artery arose as a separate artery from the aorta a short distance above the origin of the celiac axis. It supplied branches to the left adrenal gland and the left side of the diaphragm, and its terminal branches supplied the lesser curvature of the stomach.

There were four arteries which supplied the left kidney. They all arose from the left lateral side of the aorta below the superior mesenteric artery. The highest, and smallest, artery supplied the upper pole of the kidney, and the remaining three entered at the hilus. Two veins arose from the kidney and united to form the renal vein, which crossed above the aorta and entered the inferior vena cava. At the junction of the two renal tributaries was a smaller vein, which connected the renal veins with the inferior vena cava 3 cm. below the entrance of the large renal vein. This small vessel ran below the aorta. The large renal vein also received a small tributary vein from the left adrenal gland.

The inferior vena cava lay above and to the right of the aorta in its lower three quarters. The other smaller veins accompanied and corresponded to their companion arteries.

Nerves: The sympathetic trunk entered the abdominal cavity through the large hiatus in the diaphragm previously described. As the trunk entered the abdomen it was completely hidden by the right adrenal gland (fig. 13). When the adrenal gland was reflected medially, the sympathetic chain was clearly seen (fig. 14). Directly under the gland the sympathetic chain broke up into three terminal strands. The upper two entered the adrenal gland on the right, while the lowest, and largest, strand continued medially and downward along the lateral margin of the vertebral column. Detailed dissections of the various abdominal plexuses were not attempted.

Pelvis.—Bladder: There were a well developed medial umbilical fold and two large, well developed lateral umbilical folds. The bladder was normal and followed the usual anatomic descriptions. There was a remnant of a structure on the right side of the bladder that seemed to correspond to the ureter on the left. This cordlike structure extended along the posterior abdominal wall on the right side to approximately 1.6 cm. above the level of the bifurcation of the aorta, where it seemed to be gradually lost in the underlying fascia. Its lower part entered the lateral angle of the bladder. The reflection of the peritoneum followed the usual descriptions with few exceptions. On the right side, because of the presence of the peculiarly elongated

ovary and uterine tube, it reflected around the right side of the uterus and then flattened out over the lateral pelvic and abdominal wall. Because of a poorly developed broad ligament on the right, the uterus, the left ovary and the tube were pulled to the left. A short mesovarium was present on the left. The rectum also had a short mesentery in its upper part. Aside from these variations the peritoneal reflections followed the usual descriptions.

Genital Organs: The left ovary was of normal size and shape. The long axis of the ovary was directed nearly vertically, and the uterine tube lay along its lateral margin. The fimbriated extremity of the tube was directed superiorly; inferiorly the tube entered the "apex" of the uterus. The uterus was of moderate size, 3.3 cm. long, 0.8 cm. from side to side and 1.6 cm.

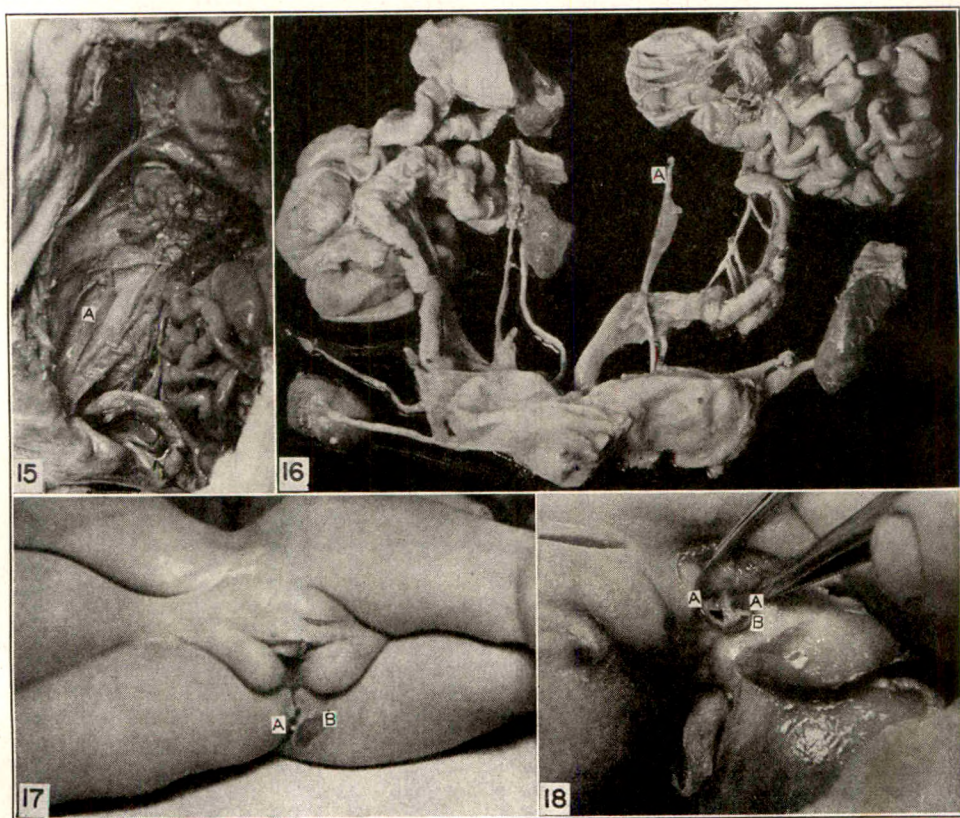
The right uterine tube gradually decreased in size as it approached the pelvis; it entered the right lateral side of the uterus about 1 cm. below the left tube. The vagina was fusiform when viewed from the front. The fornices were poorly developed.

Blood Vessels: The blood vessels conformed to the usual descriptions. There was a relatively large middle sacral artery that extended along the posterior pelvic wall to anastomose with a similar artery in the right twin.

Nerves: A detailed dissection of the nerves was not made; those encountered and dissected were normal.

STRUCTURES AT POINT OF FUSION

It is considered best to describe for the twins jointly those organs which lay at the point of fusion. Since



Figs. 15 to 18.—15, abdominal viscera after the peritoneum had been removed. Note the exposed ovary and tube on the right side (*A*). 16, organs of the genitourinary systems and the alimentary tracts of the two infants. *A* represents the anomalous right uterine tube and ovary which were present in the left twin. Note the union of the two urinary bladders. 17, external genitalia of the twins. Notice the difference in size of the labia majora. The clitoris was single, and there was a single pair of labia minora. The anal opening is labeled *A*. *B* is an area of ulceration. 18, external genitalia of the twins, showing the single vestibule. *A* and *B* represent the urethral and vaginal orifices of the right and the left twin respectively. The anal opening is plugged with cotton.

anteroposteriorly. The fundus was peaked, and the left uterine tube entered at this apex. The walls of the uterus in this twin were extremely thin. While there was no recognizable ovary or tube on the right side in the pelvic region, an odd structure, previously described, was observed on the posterior abdominal wall (fig. 13). On histologic examination it was found to be an ovary and a tube. Figure 16 shows this structure dissected out. The long, thin portion at the upper part (fig. 16) was the uterine tube. The ovarian tissue (fig. 16) extended from the widest part down to the bifurcation at the lower end of the structure.

this fusion was in the pelvic area the description will include the external genitalia and the spine.

External Genitalia: Figure 17 shows the region of the external genitalia. Apparently there were two distinct pubic eminences, located over the respective symphyses. Four rounded and distinct masses of tissue were present in the genital region and corresponded to the labia majora. The right labium of the right twin and the left labium of the left twin were in close relationship to the pudendal cleft and were larger than the other two labia. The left labium of the right twin and the right labium of the left twin lay at a distance

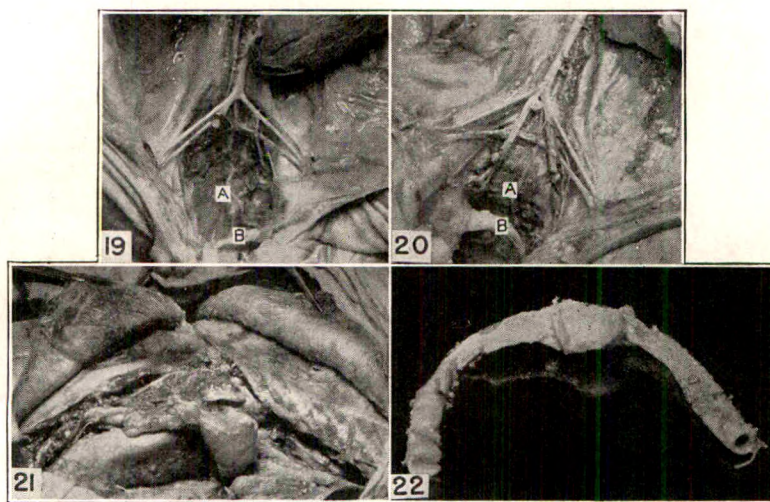
of 1 cm. from the pudendal cleft. Here the distinct pairing of the organs seemed to end, and the remaining external structures were single.

For convenience in description, the terms above, upward, etc., will be applied to the position toward the top of the accompanying photographs. One pair of labia minora was located in the midline at the point of fusion. The long axis of the labia was roughly parallel to the plane of fusion. Each labium minus measured approximately 5 mm. in length and was placed along the anterior half at the side of the vestibule. There was a single clitoris, which was located beneath the anterior labial commissure, almost entirely hidden by the anteromedial ends of the labia minora. The prepuce and the frenulum of the clitoris were well developed.

Below the clitoris was a semicircular-shaped vestibule, the base of which was directed toward the clitoris. This vestibule had a well defined and slightly raised median septum, on each side of which were two wedge-shaped orifices (fig. 18). The two upper orifices were

entire sacrum of the right twin and about half the sacrum of the left twin. The coccyx was common to both infants. The ilia were not fused. The posterior superior spines of the ilia were approximately 4.6 cm. apart. The posterior superior spine was 2.7 cm. from the midpoint of the coccyx in both twins. A large meningocele was present and was contributed to by each twin. The meningocele was directed posteriorly and superiorly (fig. 21). A laminectomy of the lumbar vertebrae was performed, and the meningocele and a section of the cord was removed from each twin. The cord had been reduced to a hollow tubular structure, with the walls about 1 mm. thick (fig. 22).

When the surface of the skin was cut to separate the twins, a heavy fascial layer was encountered. This layer extended between the two infants, and a separation of the two buttock regions could be made by blunt dissection. The only structures encountered bridging the area were a very few nerve fibers. On the inside of the pelvis the two peritoneal cavities were separated from each other by a vertical fascial septum. In this



Figs. 19 to 22.—The pelvic cavities of the right (19) and left (20) twins have been photographed to show: A, the middle sacral artery of each twin (these arteries anastomose at the point of fusion of the twins); B, the heavy connective tissue cord that was embedded in the fascial septum which separated the peritoneal cavities of the twins. 21, posterior view at the point of union of the twins. A laminectomy was done to expose the meningocele and cords. 22, cords with the common meningocele. Note the extremely thin walls of both cords. The cord of the right twin is on the left side of the photograph.

about half as large as the lower ones and were the external urethral openings for the right and left twins. The two larger lower openings were the external vaginal orifices. Approximately 2 cm. below the lower boundary of the vestibule was a single anal opening (fig. 18). On closer examination a median septum, formed by the adjoining walls of the rectums of the two infants, was found just inside this opening.

During the course of the dissection of the pelvic organs a heavy fibrous cord (5 cm. long) was encountered, which crossed the pelvic cavity at the plane of fusion (figs. 19 B and 20 B). Its diameter, approximately 6 mm. at the origin, decreased rapidly. The cord extended deep to the pelvic organs and was attached to the posterior lateral wall. Histologic examination showed it to be muscle, fascia and vessels. The rest of the plane of fusion was filled with a thin fascia.

Spine.—Examination of the twins from the back showed a leaking meningocele with accompanying spina bifida. The spina bifida involved the sacral areas: the

septum the heavy fibrous cord, previously described, was embedded.

This completed the gross dissection study. Further data on histologic observations, handprints and footprints were collected.

COMMENT

The occurrence of pathologic specimens among human embryos is not as infrequent as one might think from the number of abnormalities and monstrosities seen at birth. F. P. Mall,¹ in examining 1,001 specimen embryos and ova, found nearly 40 per cent of them pathologic. Usually, however, since most of the abnormalities are not compatible with growth and develop-

1. Mall, F. P.: On the Frequency of Localized Anomalies in Human Embryos and Infants at Birth, *Am. J. Anat.* 22:49 (July) 1917.

ment, the embryos are aborted early in pregnancy. Mall found only 5 monsters carried to term among 1,001 specimens examined.

Reports on Pygopagus Human Twins.—A number of pygopagus twins have been described in the literature, but unfortunately no descriptions of complete dissections are available. They have been described more as curiosities or in consequence of a wish to record briefly the superficial anomalies and psychologic findings than with the object of giving an embryologic interpretation. In this discussion mention will be made of only the better known pygopagus twins. The Blazek twins were described by Sir John Bland-Sutton² and Benjamin H. Breakstone.³ These twin girls, of Bohemian origin, were joined by their sacra and were double except for the genitalia and the anus. The vulva was single but received two urethras from separate bladders. They lived to be adults, and Rosa gave birth to a male child.

Another case of conjoined twins of this type (Simplicio and Lucio Godena) was reported by Louis Sullivan.⁴ These twins were boys, aged 10 years at the time Sullivan examined them. They were born on the island of Samar, Philippine Islands, of mixed Malay stock. They were considered to be identical twins and were joined at the buttocks. While the rectum was common to the twins, the genital organs were normal.

The Hilton twins, examined and reported by Newman,⁵ were joined in the same manner as the Blazek twins. The Hilton twins were girls. Several pygopagus twins were mentioned by Newman, but no details were given.

Theories of Causation.—It is generally conceded that the production of monsters is not due directly to germinal or hereditary causes but probably results from factors which affect or disturb the usual pattern of the development of normal ova.

Various experiments have been carried out on the lower animals whereby monsters were produced by certain environmental changes. Stockard⁶ suggested that a change in the supply

of oxygen was probably the most likely factor, particularly in the placental group. This change, occurring at a crucial period in the development of the embryo, would arrest the normal pattern of development and might account for the double gastrulation or blastopore formation, resulting in the formation of two axes instead of the usual one. Stockard has also been able to produce double monsters in fish by lowering the temperature at a critical period. In cases of placental groups the possibility of extreme changes in temperature must be ruled out. It has been possible experimentally (Wilson,⁷ Loeb⁸ and others) to separate the two primary blastomeres with resulting formation of twins. Spemann⁹ was able to produce double monsters by partial constriction of the egg during later stages of blastula or gastrula. Wilson¹⁰ and Conklin¹¹ found, however, that not all species produce complete twins when the blastomeres are separated.

It is hard to conceive of factors capable of producing comparable separations, either complete or partial, in an environment as protected as that in the uterus. Nevertheless, Wilder's¹² "blastotomy theory" of the formation of double monsters was based on this concept. Newman¹³ expressed the opinion that twinning is due to fission of a single embryonic axis followed by a secondary partial fusion. Witschi¹⁴ recognized overripeness of the egg as a causative factor in the production of identical and conjoined twins. Overripe eggs are no longer capable of the normal axiate organization. Instead it often happens that two or more secondary points of gastrulation and two or more embryonic axes result. In placental animals this condition seems more plausible as a causative factor than some of the previously mentioned environmental

7. Wilson, E. B.: Amphioxus, and the Mosaic Theory of Development, *J. Morphol.* **8**:579 (Aug.) 1893.

8. Loeb, J.: Beiträge zur Entwicklungsmechanik der aus einem Ei entstehenden Doppelbildungen, *Arch. f. Entwicklgsmechn. d. Organ.* **1**:453, 1895.

9. Spemann, H.: Entwicklungsphysiologische Studien am Triton-Ei: I. *Arch. f. Entwicklgsmechn. d. Organ.* **12**:224, 1901; II, *ibid.* **15**:448, 1902; III, *ibid.* **16**:551, 1903.

10. Wilson, E. B.: Experimental Studies on Germinal Localization: I. The Germ-Regions in the Egg of Dentalium, *J. Exper. Zool.* **1**:1 (May) 1904.

11. Conklin, E. G.: Mosaic Development in Ascidian Egg, *J. Exper. Zool.* **2**:145 (May) 1905.

12. Wilder, H. H.: Duplicate Twins and Double Monsters, *Am. J. Anat.* **3**:387 (Sept.) 1904.

13. Newman, H. H.: Twin and Triplet Chick Embryos, *J. Hered.* **31**:371 (Sept.) 1940.

14. Witschi, E.: Appearance of Accessory "Organizers" in Overripe Eggs of the Frog, *Proc. Soc. Exper. Biol. & Med.* **31**:419 (Jan.) 1934.

2. Bland-Sutton, J.: Rosa-Josepha Blazek: The Bohemian Twins, *Lancet* **1**:772 (April 15) 1922.

3. Breakstone, B. H.: The Last Illness of the Blazek (Grown-Together) Twins, *Am. Med.* **28**:221 (April) 1922.

4. Sullivan, L.: The "Samar" Twins, *Am. J. Phys. Anthropol.* **2**:21 (Jan.) 1919.

5. Newman, H. H.: Differences Between Conjoined Twins in Relation to a General Theory of Twinning, *J. Hered.* **22**:201 (July) 1931.

6. Stockard, C. R.: Developmental Rate and Structural Expression: An Experimental Study of Twins, Double Monsters and Single Deformities, and the Interaction Among Embryonic Organs During Their Origin and Development, *Am. J. Anat.* **28**:115 (Nov.) 1921.

agents. The tendency to retain the ovum until it is overripe is possibly based on endocrine factors, which may or may not be of hereditary type.

In regard to the condition producing twinning and conjoined twins in human beings the theory advanced by Witschi seems to explain most adequately the conditions found. If retention of the egg within the follicle for a longer period than usual is assumed, the power of the egg to differentiate normally would gradually decline. When the egg is finally expelled and fertilized, instead of a single primitive streak there now develop two. In the case of pygopagus twins they are located at some distance apart, so that each begins to develop independently. Apparently the axes of the embryos are not parallel but converge caudally. Consequently, during the later course of the formation of the embryos the two neighboring sides meet and partially fuse.

Probable Embryonic Development of the S. Twins.—The peculiarities occurring in the genitourinary organs of the S. twins indicate that during development paired pronephric and mesonephric primordia were present in each twin. This is concluded from the presence of four essentially normal ovaries. The first peculiarity is encountered in the derivatives of the

metanephric blastema cords. As was previously mentioned, there was a metanephros for the right side of the right twin and one for the left side of the left twin. But evidently the adjacent metanephric primordia for the left side of the right twin and the right side of the left twin must have been fused into a common midline mass. With growth and folding of the walls of the body, most of this single metanephros must have become included in the body of the right twin. The presence of the partial ureter in the left twin is not in disagreement with this interpretation, since embryologically it is a derivative of the mesonephric duct.

In conclusion, the anatomic peculiarities of the S. twins indicate that the adjoining nephrogenic blastema cords fused at about the level of the twenty-eighth somite and the spinal tubes at about the thirty-second somite. In other words, fusion of the separately started embryos occurred during the fourth postovulatory week of development.

Members of the department of Pediatrics of the State University of Iowa were primarily responsible for making the twins available to me for study. Captain C. B. Hall, who delivered the twins, provided information concerning the placenta and the delivery. Dr. R. J. Terry gave criticisms and suggestions on the anatomic portion of the paper, and Dr. Emil Witschi gave suggestions and aid in interpreting the embryologic material.

ANOMALY OF THE PERIPHERAL VESSELS IN A NEWBORN INFANT

HOWARD A. WEINBERGER, M.D.

NEW YORK

The present paper reports a microscopic anomaly in the peripheral vascular system of an infant in conjunction with a death anatomically attributed to multiple small focal hemorrhages in association with formation of abscesses. A review of the literature fails to reveal any report of lesions resembling those about to be described.

of vomiting of one week's duration. The infant, born at full term, had been delivered by forceps and at birth weighed 6 pounds, 13 ounces (3,090 Gm.). He was a first child. The parents were living and well, and no history of familial disease was elicited.

Physical Examination.—Physical examination revealed a poorly nourished infant weighing 5 pounds 14 ounces (2,665 Gm.) and appearing neither acutely ill nor dehydrated. A peanut-sized tumor mass was

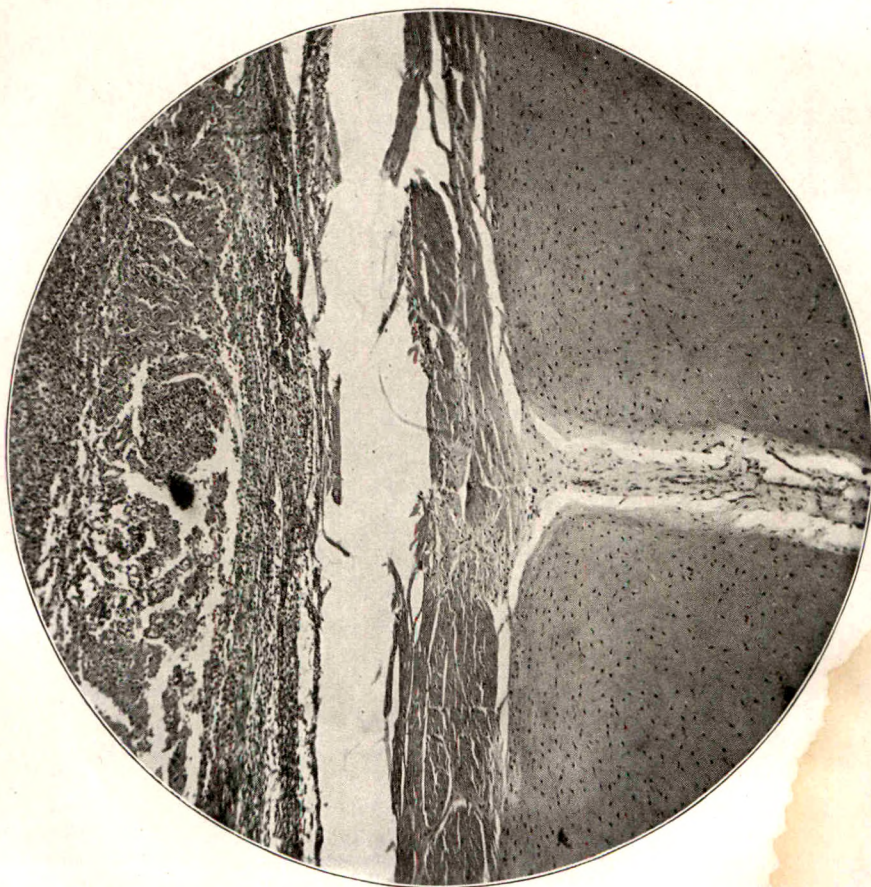


Fig. 1.—Hematoxylin and eosin stain; $\times 70$. Hemorrhages and formation of abscesses in muscle and connective tissue adjacent to costal cartilage.

REPORT OF A CASE

A two week old white boy was admitted to the children's division of the hospital on June 26, 1944 because

From the Achelis Laboratories and the Abraham Jacobi Division for Children of the Lenox Hill Hospital.

Dr. Jerome S. Leopold gave permission to investigate this case. Drs. George L. Rohdenburg and Rudolf M. Paltauf gave stimulating and constructive criticism in the study of the material.

palpable in the right upper quadrant of the abdomen. There were no other positive findings. The patient's temperature on his admission to the hospital was 98.4 F.

Course.—Observation during the next forty-eight hours demonstrated the vomiting to be projectile. Few of the feedings were retained. A clinical impression of hypertrophic pyloric stenosis was confirmed by roentgenographic studies made after administration of barium sulfate. Two days after the patient's admission a Ramstedt operation was performed, an incision being

made in the right upper quadrant. The peritoneum was closed with continuous plain catgut, the fascia with interrupted chromic catgut and the skin with interrupted silk sutures.

For the following forty-eight hours the infant continued to do poorly and vomited persistently. On the second postoperative day the operative site was exposed and a dehiscence of the wound with evisceration of a loop of small bowel identified. Under general anesthesia the wound was closed with through and through interrupted braided silk sutures.

After this procedure the infant continued to do poorly. Nutrition per os was inadequate, and daily infusions of

blood and suddenly died. The clinical impression was that the cause of death was sclerema.

Autopsy.—Gross Examination: A postmortem examination performed the day of death revealed the following data: The body was poorly developed and poorly nourished. There was a partly healed upper right rectus incision. The skin showed no alterations on gross examination. At several of the distal interphalangeal joints of the fingers and the toes there were slightly elevated purplish red areas about 0.5 cm. in diameter. In the soft tissue and the muscle overlying the costal cartilages near the sternal margin were purplish red areas revealing on cross section circumscribed hemor-

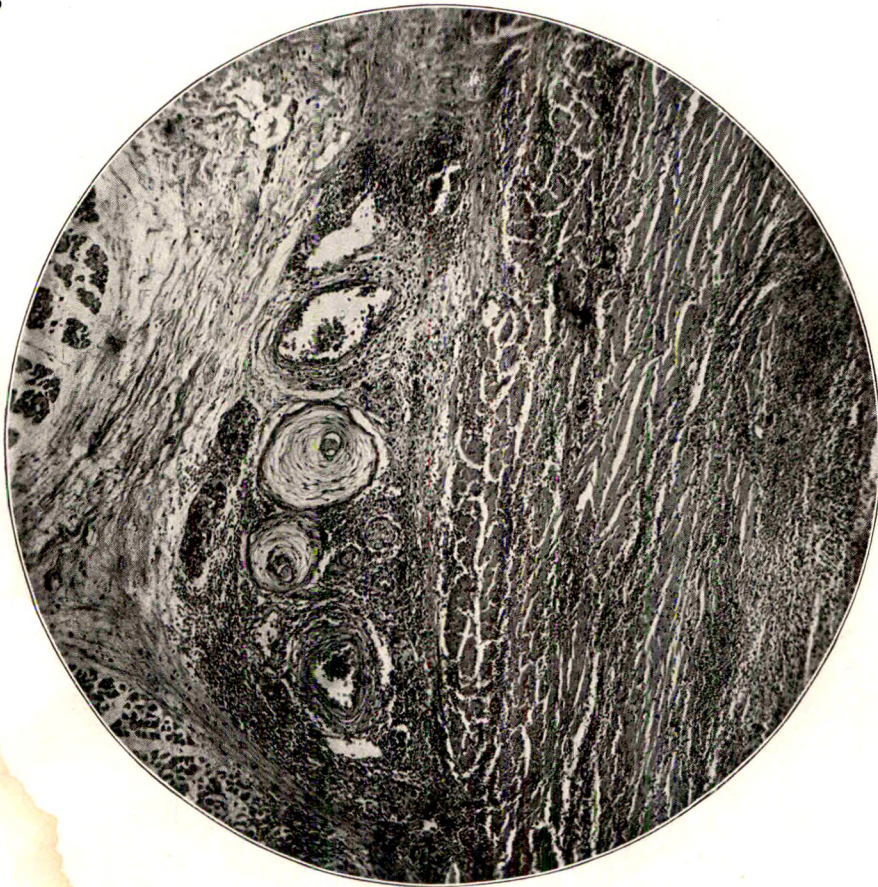


Fig. 2.—Hematoxylin and eosin stain; $\times 70$. Hemorrhage and obliterative arteritis in muscle over costal cartilage.

plasma and of sodium chloride solution were administered in addition to a single transfusion of whole blood.

On the third postoperative day after closure of the disrupted wound a brawny, generalized edema was recorded, and this was more conspicuous on the following day. At this time the urine showed an occasional leukocyte and red cell. An analysis of the blood showed hemoglobin 14.2 Gm. per hundred cubic centimeters (95 per cent), red blood cells 4,900,000 and white blood cells 4,800, with 41 (8) per cent neutrophils (33 per cent mature and 8 per cent immature), 57 per cent lymphocytes and 2 per cent eosinophils. A temperature range of 96 to 102 F. was noted during this period.

The steady downhill course continued, and on the tenth day after admission to the hospital (the sixth day after the second operative procedure), while being fed, the infant grew cyanotic, coughed up a small amount of

rhages surrounding a small amount of turbid brown, purulent-appearing material. A few loops of small intestine were loosely united by thin, easily separated adhesions; the peritoneal surfaces were otherwise smooth and glistening throughout. A 2 cm. longitudinal surgical incision was present on the anterior part of the pylorus, and this extended completely through the muscularis, the cut margins of which were bulging; there was no fibrin reaction and no scar formation. The lungs showed extensive collapse posteriorly. Examination of the remaining parenchymatous organs and of the gastrointestinal tract revealed no gross abnormalities.

Microscopic Examination: Microscopic histologic examination demonstrated the following data: Sections through the lungs revealed focal and diffuse interstitial, intra-alveolar, and subpleural extravasations of blood. Patchy areas of atelectasis were present. The vessels

appeared to be normal. In the myocardium there was noted a single abscess consisting of a central necrotic zone rich in polymorphonuclear leukocytes, and this was surrounded by a thin, fibrous stroma infiltrated with small round cells and polymorphonuclear leukocytes. In the liver there was diffuse sinusoidal congestion; the vessels were not remarkable. The fibrous elements of the spleen were increased in number; the vessels were normal. Sections through the pylorus demonstrated the mucosa to be intact. The muscularis was markedly thickened, the margins of the surgical incision were well outlined and there was no inflammatory response or attempt at fibroblastic bridging of the defect; in the serosa a few large wandering cells were seen. In the renal cortex the glomerular tufts were delicate. The

ations, and many of the arterioles here showed varying degrees of obliterative arteritis, from adventitial thickening and chronic inflammatory infiltration of cells to intimal proliferation and fibrous occlusion (fig. 2). Finally, in the loose connective tissue overlying the intact bundles of muscles there were several of the discrete, compact, endothelioid-like masses of cells so conspicuous in the skin.

Study of the skin demonstrated the squamous epithelium to be thinned out and the rete pegs short and inconspicuous; beneath were the usual appendages of the skin. The stroma of the corium was much thickened, sclerosed and hyalinized and supported in its depths many elongated finger-like retractile cords composed of closely packed cells supported by a thin capillary stroma

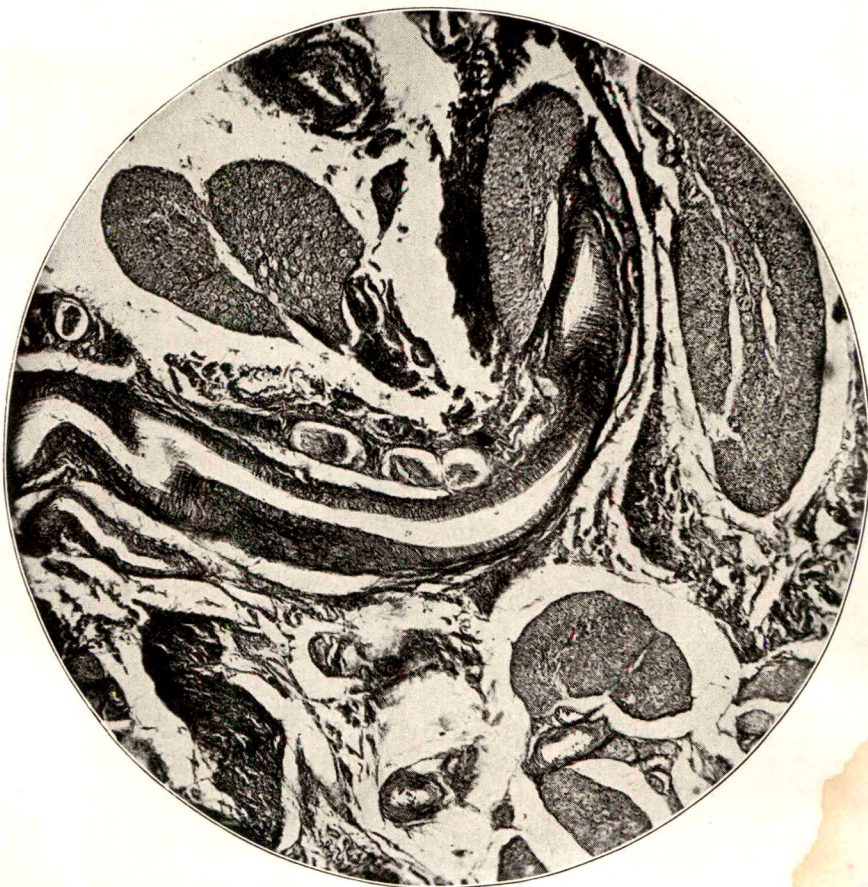


Fig. 3.—Mallory stain; $\times 70$. Demonstration of the endothelioid-like cell masses in the deep layers of the skin. Also present in the connective tissue of the costal cartilage region and in the serosal fat adjacent to the pancreas.

radial arteries were congested, and in the medulla there were small and large extravasations of blood in the stroma and into the tubules. A small abscess composed of central necrotic debris and small round cells surrounded by a zone of hemorrhage was present in the medulla.

Sections through the costal cartilage demonstrated that the muscular bundles on each side of the cartilage plate were frayed and disrupted or were necrotized and infiltrated with inflammatory cells, in which polymorphonuclear leukocytes were present in abundance (fig. 1). The regions of necrosis and infiltration were irregular, in some instances extending into the underlying cartilage, which here was rarefied, necrotic or fibrosed. Hemorrhagic extravasation was uniformly present in or near the zones corresponding to these destructive alter-

(fig. 3). These cells were generally large and oval except when lining the numerous discrete blood channels, when they were elongated and resembled typical vascular endothelium; the nuclei were vesicular and occasionally elongated, and their cytoplasm was pale-staining, granular and sometimes vacuolated. No mitoses were seen, and the cords of the cells exhibited no infiltrative tendencies. The numerous small capillary channels usually contained red blood cells and generally had a diameter capable of accommodating one or two red cells. Occasionally, here and in the other regions of the body in which these structures were found the blood spaces in the cords were tortuous and dilated and did not contain blood elements. Lesions similar to those in the deep corium of the skin were present in the peripancreatic connective tissue.

COMMENT

The pathologic picture of the skin is not that of sclerema or of allied diseases.¹ Fat degeneration, trabecular thickening, needle-like crystal spaces and rosettes and granulomatous proliferation with epithelioid and giant cells were absent here. The most conspicuous feature in this case was the presence in the connective tissue of the skin and in the loose connective tissue elsewhere of peculiar discrete circumscribed processes of endothelioid-like cells channeled by multiple small and uniform capillaries. The appearance of these structures suggests that they represented embryonic vascular rests undergoing much delayed development or maturation toward formed blood channels.

Recalling the embryology of the vascular system,² one notes that the primordia of the blood vessels make their appearance extremely early in the development of the embryo. In the 24 hour old blastoderm (five segments) the area vasculosa is well outlined at the border of the vesicle. It has been demonstrated conclusively that blood vessels in the embryo have their origin in situ from the primitive mesenchymal cells, which by coalescence form blood islands. The cells of the islands become variously compressed and vacuolated to form primitive angioblastic primordia lined by young endothelium. This process occurs throughout the entire blastoderm. Shortly these independently patterned channels fuse to form intact blood vessels. It is not until considerably later, after the circulation begins, that

new vessels may arise by sprouting from pre-existing blood channels.

From an analysis of the striking pathologic changes in this infant it is difficult to find their cause and to establish interrelationships. Study of the material indicates that the cause of death was a systemic vascular insult with hemorrhage extravasation and secondary formation of abscesses in various regions and organs of the body, including the costal pericartilaginous tissues, the lungs, the kidneys and even the myocardium. Ordinarily one might assume these to be manifestations of a pyemic or an embolic phenomenon. However, there were no signs of generalized or local peritonitis, and no other focus of infection was demonstrable clinically or on postmortem examination. One cannot escape the fact that the multiple lesions of hemorrhage and necrosis with abscess formation in this case are concurrent findings with the peculiar vascular tufts composed of endothelioid-like cells. The latter structures were found in the deeper part of the corium, in the soft connective tissue of the region of the costal cartilage and in the serosal fat overlying the pancreas. One may conjecture as to the possible relationship or the common derivation of these two distinct lesions. Perhaps the entire situation represents a generalized arrested and/or delayed development of the peripheral vascular system, with the hemorrhagic phenomena a manifestation of the fragility of anatomically immature or poorly developed walls of small vessels.

CONCLUSION

A hitherto undescribed anomaly of the peripheral vascular tree was observed in a newborn infant, who died.

In reviewing the pathologic features of this case the relationship of the two vascular lesions, the one proliferative and presumably embryonic and the other destructive, is obscure.

Consideration of the embryologic aspects led to a hypothesis of embryonal maldevelopment of the peripheral vascular tree.

Lenox Hill Hospital.

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HAIR LACQUER DERMATITIS IN INFANTS FROM CONTACT WITH MOTHER'S HAIR

MILTON PLOTZ, M.D.

Assistant Clinical Professor of Medicine, Long Island College of Medicine

BROOKLYN

Dermatitis caused by hair lacquer has by now become recognized as a well defined clinical entity. The condition has been described mostly in women who use the lacquer to keep hair in place, a matter of some difficulty in the case of the present fashionable "upswept hair-do." Some instances have been reported in young children,¹ in whom the lacquer was used presumably for the same function, as a hair dressing. This communication reports 2 cases in which infants of less than a year were affected. Since the lacquer was not applied directly to the victims' hair, the diagnosis was considerably more difficult than in the usual case of this disorder.

The pathogenesis of this dermatitis has been studied in detail by Schwartz.² Hair lacquer in use before the war contained shellac, which seems to have produced dermal reactions very seldom. Since then, synthetic resins, combinations of rosin and maleic anhydride, have been substituted for the unobtainable shellac. The direct action of the chemical has been enhanced by the extremely high or extremely low p_H of the finished commercial product.

REPORT OF CASES

CASE 1.—A white girl 10 months old was seen incidentally to the examination of her mother for a cardiac condition. The mother complained bitterly that she had treated the child for "eczema" of the face since the age of 2 months without success. Local therapy,

From the Cardiac Clinic, Bushwick Hospital, Brooklyn, N. Y.

1. Epstein, S.: Contact Dermatitis Caused by Hair Lacquer Pads, J. A. M. A. **123**:409 (Oct. 16) 1943.

2. Schwartz, L.: An Outbreak of Dermatitis from Hair Lacquer, Pub. Health Rep. **58**:1623 (Oct. 29) 1943.

changes in diet, allergy tests of all sorts had been tried to no avail.

Examination of the infant revealed a dermatitis of the inner sides of both forearms, especially the right. The external aspects of the arms and forearms were less involved. The right side of the neck, both cheeks and part of the forehead were involved. No unexposed portions of the body were affected. The lesions were red, swollen, poorly defined and somewhat crusted and vesiculated. The child seemed distressed by the skin condition and cried a great deal.

When the mother picked up the child, it was observed that the child's skin was brought into close contact with the mother's lacquered hair. The first published reports of dermatitis due to lacquer had just appeared, and the possibility that the infant might have this condition suggested itself. The material in the lacquer pad used by the mother was employed in a patch test, which elicited a strongly positive reaction. The dermatitis subsided quickly when the mother discontinued the use of lacquer. The condition disappeared within a week and has never returned.

CASE 2.—A boy 6 months old was brought for cardiac examination because the family physician had found a murmur.

Examination revealed a congenital cardiac lesion, probably a patent interventricular septum. There was a crusty, erythematous dermatitis involving the forearms, one cheek, most of the forehead and temples and the back of the neck. This condition had not responded to changes in diet or to medication prescribed by the pediatrician and a consulting dermatologist.

In the light of my experience with the first patient, the possibility of a similar pathogenesis was considered at once. A patch test with the mother's hair lacquer was strongly positive. In this case, too, the eruption disappeared as soon as the mother adopted another hair dressing.

SUMMARY

In 2 infants dermatitis was caused by hair lacquer used by the mother.

In each case the possibility of this dermatitis had not been considered because lacquer had not been applied directly to the infant's hair.

1120 Church Avenue, Brooklyn 18.

Abstracts from Current Literature

Metabolism; Infant Feeding Milk and Other Foods

STUDIES OF THE NUTRITIONAL STATE OF CHILDREN IN UNOCCUPIED FRANCE IN THE FALL OF 1942. HAROLD C. STUART, J. Pediat. 25:257 (Sept.) 1944.

Studies of the nutritional state of children were organized by the American Red Cross in connection with its program for distribution of milk in unoccupied France and were carried out at the medical schools of Lyon, Clermont-Ferrand and Montpellier, at the Institut de Recherches d'Hygiène in Marseille and at a state hospital in Monaco. The same examination was carried out at each center on a group of 80 to 100 children, who were then to receive from the American Red Cross a supplement of milk at school. It was planned that the examination should be repeated on the same children at four month intervals during the period of supplemented feeding. The children selected were between 10½ and 11½ years of age and were attending schools which were considered to be most representative of general conditions in their communities. An American Red Cross record form was prepared, which required only checking of code numbers to indicate the evaluation of observations made at examinations. The latter included items from clinical examinations, body measurements and study of roentgenograms and blood samples.

The data reported in this article were obtained from records and roentgenograms of 134 children, especially of 35 girls and 53 boys in the 11 year age group, in Marseille, which the writer had an opportunity to study while in detention in France, prior to being taken to Germany for internment. The laboratory determinations were not available at this time, and the numbers of children studied were not sufficient to justify tabulation of the clinical findings; so the report deals principally with body measurements obtained from roentgenograms and evaluation of the latter from the standpoint of osseous development and of nutritional state. Tables are included which give mean values for all the measurements and the deviations of these from American norms. The body measurements used were weight, height, chest circumference and pelvic breadth. The measurements taken from an anterior-posterior view of the leg area were length of tibia, breadth of calf, breadth of tibia, breadth of muscle and breadth of skin and subcutaneous tissue.

Except for breadth of pelvis of girls, the mean values for all measurements of the children in Marseille were smaller than for the American children chosen for comparison. Body weight was considerably less than would be expected normally after making corrections for size and build. As indicated by the roentgen measurements, this was due both to lack of skin and subcutaneous tissue and to slight muscular development. A comparison of these results with the results of similar studies in Marseille eighteen months earlier failed to demonstrate any greater deficit in the averages for measurements of soft tissues, despite continued underfeeding. In both periods 6 year old children were found to be more nearly up to American standards in these measurements than were 10 or 11 year old children. No roentgenographic evidences of active rickets or of scurvy were found, but a few roentgenograms showed faulty mineralization.

When these roentgenographic measurements were compared with the norms, given in the *Atlas of Skeletal Maturation* presented by Todd, both the boys and the girls in this French series were found to be on the average approximately one year behind expectancy in osseous development, as was the case with the children studied early in 1941 in Marseille. A figure is presented giving the deviations from the norms in mean anatomic ages for all measurements studied and for both sexes. This shows that the French children, according to most of these criteria, were between one and one and one-half years behind the American children with whom they were compared.

The article closes with a general review of the nutritional situation in unoccupied France at the end of 1942. The evidence appears to be that infants and young children have not suffered as much as older ones and that those over 12 years old especially have been showing evidences of a general type of under-nutrition in ever increasing numbers. By this are meant lack of weight, failure to gain and grow normally, lack of vigor and ready fatigue, mild anemia and inadequate storage of vitamins in the blood. These findings would be expected on the bases of dietary surveys, which indicate low total calories, low level of total protein and especially of animal protein, low level of calcium and lack of certain vitamins. There had, however, been little increase of outspoken deficiency diseases, and it did not appear that in any considerable percentage of children at any age health had been profoundly affected, life endangered or development more than moderately retarded. Under these circumstances it was felt that the supplement of 259 Gm. of milk which the American Red Cross was then about to distribute to the children from 10 to 14 years of age would be ideally suited to retard if not to prevent further deterioration of their nutritional state.

STUART, Boston.

THE PROTECTIVE DIET. RUTH PYBUS, Edinburgh M. J. 51:21 (Jan.) 1944.

The author, who is sister dietitian at the Royal Infirmary, emphasizes the need for a protective diet, especially for school children. A common problem in the home is an adequate supply of vitamin C; the amount furnished at home often needs to be supplemented by approximately 40 mg. at the school luncheon. Pills or capsules of ascorbic acid contain only the vitamin and therefore are not to be compared with green vegetables. When citrus fruits are not available, raw spring cabbage is used; the latter is twice as potent, though not so well liked. Vegetables are useful raw and also when correctly cooked if not kept hot too long. The content of vegetable broth is somewhat variable. The author gives the following figures for vitamin C in vegetables:

Vegetable broth10 to 15 mg. in ⅓ pint (20 cc.)
Cooked new potato (not mashed)25 mg. in 5 ounces (142 Gm.)
Lightly cooked cabbage16 mg. in 3½ ounces (99 Gm.)
Watercress5 mg. in ⅓ ounce (9 Gm.)

Tomato and other raw salads may well be alternated, along with citrus fruits. The need for calcium is met by milk given both at home and at school. For young children vitamins A and B will be provided by the use of cod liver oil, dried egg and milk; older children will like fatty fish, the amount of vitamin A being augmented by carrots, green vegetables and liver.

Nursery schools can be of teaching value to promote good feeding habits. Children enjoy their foods much better if they have had an adequate mixed diet since early life.

NEFF, Kansas City.

THE BANANA (*MUSA PARADISIACI* OF LINNAEUS) IN INFANTILE FEEDING. MERCEDES CHÁVES ARANGO, Bol. Soc. cubana de pediat. **15**:253 (May) 1943.

The author divides her work into three parts: (1) historical notes; (2) botanical considerations, and (3) discussion of the use of bananas and banana powder in the diet of Cuban children, both normal and sick.

She cites experiments on rats fed with banana to determine the vitamin B₂ content and the pH of feces, the number of colonies in agar cultures of feces, etc. Because of its pleasant flavor, its richness in carbohydrates, vitamins and minerals and its high caloric value, she advises its use in the diet of normal infants and children and especially in the treatment of marasmus and celiac disease.

KEITH, Rochester, Minn.

THE PLANTAIN (*BANANA*) (*MUSA PARADISIACA* OF LINNAEUS) IN INFANT FEEDING. L. E. C. FONSECA, Bol. Soc. cubana de pediat. **15**:343 (June) 1943.

This article discusses the use of the plantain, a banana commonly used in Cuba. The varieties of the banana are mentioned, and their chemical compositions, both when green and when ripe, are outlined. The banana powder is also described. The use of banana is recommended in the treatment of infant diarrhea, bacillary dysentery, typhoid and celiac disease, as well as in the feeding of normal infants. Twenty-six illustrative cases are outlined.

KEITH, Rochester, Minn.

RAW COW'S MILK IN THE NOURISHMENT OF THE CHILD: ITS ADVANTAGES AND DISADVANTAGES. FÉLIX BURÉS MOLINA, Bol. Soc. cubana de pediat. **15**:372 (June) 1943.

This is a discussion of the use of cow's milk in infant feeding. The details of the composition, the grading and the handling of the milk are given, with considerable discussion of the bacterial content.

KEITH, Rochester, Minn.

NUTRITIONAL UTILIZATION OF THE OIL OF CHESTNUTS FROM PARÁ. M. L. DE OLIVA COSTA, Horo méd., Rio de Janeiro **1**:31 (Feb.) 1943.

After previous studies done by Dr. Dante Costa and his co-workers in the laboratory, the author performed experiments in cooking with Brazil nut oil as a substitute for fats, olive oil and other vegetable oils, fats commonly employed in human food.

The experiments consisted in the preparation of several dishes used in Brazil, such as beefsteaks, eggs, and rice and beans, fried or cooked with the oil obtained from Brazil nuts, with absolutely satisfactory results as to taste and good appearance of the food. Brazil nut oil was successful too in the preparation of salads.

Under present wartime conditions the utilization of Brazil nut oil in the preparation of food will help solve the problem of the shortage of edible fats.

The oil will be obtained by compression, giving incidentally another product, partially defatted Brazil nut flour, a useful protein food already studied and proposed by Dante Costa and S. Mota.

It should be possible to produce the Brazil nut oil at a low cost.

AUTHOR'S SUMMARY.

PROBLEMS OF NUTRITION AND DIETARY REQUIREMENTS IN CHINA. J. HENG LIU and C. K. CHU, Chinese M. J. **61**:95 (April-June) 1943.

Beriberi is regarded as the most prevalent of the deficiency diseases in China. Xerophthalmia and keratomalacia are not at all rare; this is also true of such deficiency diseases as rickets, tetany and scurvy, though these may be so mild that the patients do not come to the physician. Because of the prolonged deficiency in protein feeding due to the war, nutritional edema is on the increase.

The authors state that preschool children and infants should be divided into two age groups. They give five tables of suggested foods, four of which are planned for infants, preschool children, school children and youths respectively. For each group the number of grams of foodstuffs in general and of calcium and protein and the calories furnished by each food are enumerated. As would be expected, youths are supplied somewhat more abundantly than adults. Infants under 6 months of age are excluded from this study, because in China all mothers are expected to nurse infants of this age.

A great problem in China, even after the war, will be the danger arising from widespread use of milk, since it is so perishable a commodity in that country. The attempt will be made to get along without fresh milk and other fresh dairy products and to produce powdered milk in quantity for supplying the food elements needed by growing infants and children.

NEFF, Kansas City.

Vitamins; Avitaminoses

ON THE ISOLATION AND PROPERTIES OF THE FLUORESCENT FACTOR F₂ FROM HUMAN URINE. VICTOR A. NAJJAR, VIRGINIA WHITE and DWIGHT B. MCNAIR SCOTT, Bull. Johns Hopkins Hosp. **74**:378 (June) 1944.

When the body is adequately supplied with nicotinic acid a highly fluorescent compound, F₂, apparently derived from a precursor, can be obtained from the urine by appropriate treatment. The identity of the precursor has not been established. The substance F₂ appears to be a butyl ether of N-methyl nicotinamide alphacarbinol.

LYTTLE, Los Angeles.

THE LABORATORY DIAGNOSIS OF NICOTINIC ACID DEFICIENCY: AN IMPROVED PROCEDURE FOR THE DETERMINATION OF F₂ (N-METHYL NICOTINAMIDE DERIVATIVE) IN URINE. VICTOR A. NAJJAR, Bull. Johns Hopkins Hosp. **74**:392 (June) 1944.

A modification of the original Najjar-Wood procedure for the estimation of the fluorescent factor, F₂, is described.

In adults with an oral load of 100 mg. of nicotinamide an excretion of less than 2,100 micrograms of N-methyl nicotinamide chloride in four hours may be significant of depletion.

LYTTLE, Los Angeles.

A CASE OF PELLAGRA DEVELOPING ON A HOSPITAL WARD IN A PATIENT RECEIVING VITAMIN B COMPLEX. DEAN W. ROBERTS and VICTOR A. NAJJAR, Bull. Johns Hopkins Hosp. **74**:400 (June) 1944.

Pellagra developed in a 12 year old girl who was under observation in the hospital and was receiving a preparation of vitamin B complex at the time.

It is pointed out that certain commercial yeast extracts do not supply sufficient quantities of nicotinic acid.

AUTHORS' SUMMARY.

THE ANTI-BLACK TONGUE ACTIVITY OF N-METHYLNICOTINAMIDE CHLORIDE. VICTOR A. NAJJAR, MARGARET M. HAMMOND, MARY ALLEN ENGLISH, MARIA B. WOODEN and CAROLYN C. DEAL, Bull. Johns Hopkins Hosp. **74**:406 (June) 1944.

N-methylnicotinamide chloride has been shown to be effective in preventing as well as curing black tongue in dogs. Its possible value in human pellagra is suggested. The suggestion is advanced that the F₂ nucleus (N-methyl pyridine B-carboxy-) may be the active anti-pellagra vitamin.

AUTHORS' SUMMARY.

CONGENITAL AND INFANTILE BERIBERI. DAVID W. VAN GELDER and FRANCES U. DARBY, J. Pediat. **25**:226 (Sept.) 1944.

A brief review of the literature on states of thiamine deficiency in infants is presented. The infantile form of beriberi usually develops when infants are 2 to 3 months of age; the vast majority of babies affected are breast fed. The manifestations in infants are protean: There may be anorexia, abdominal distention or tenderness, vomiting, oliguria, edema, cardiac enlargement, dyspnea, cyanosis, aphonia and even convulsions. The response to administration of thiamine hydrochloride is often extremely rapid.

A case of congenital beriberi is reported. The mother exhibited slight edema during the last trimester of her pregnancy. Because of edema her intake of fluids was limited, but in addition she voluntarily limited her diet mainly to fruits. The infant was born cyanotic and dyspneic and became almost aphonic. The heart rate was extremely rapid, and a roentgenogram of the chest showed a heart which occupied over 75 per cent of the thoracic cavity. A spectacular clinical improvement, with marked reduction in the size of the heart followed the use of large doses of thiamine hydrochloride (150 mg. daily) administered parenterally. An electrocardiogram taken early during the illness showed deviation of the axis to the right and low voltage in all leads. A subsequent electrocardiogram, after adequate treatment with thiamine hydrochloride, was normal.

Assays of the thiamine in the urine and determinations of the levels of dextrose, pyruvate and lactate in the blood, both fasting and following the ingestion of dextrose, were done on the mother after she had been restricted for a period to her antepartum diet. These tests were then repeated after a period during which she received an adequate diet. All these tests were indicative of a state of thiamine deficiency in the mother during the period of dietary restriction.

It is considered that in some instances congenital idiopathic cardiac hypertrophy or status thymicolympathicus may actually be unrecognized congenital or infantile beriberi. Infants with large hearts in whom no valvular or congenital lesion can be demonstrated

should be given large parenteral doses of thiamine hydrochloride as a therapeutic test.

Pregnant or lactating mothers should be provided with an adequate intake of vitamin B. If the maternal diet is suboptimal, nursing infants should receive additional vitamin B. VAN GELDER, Baton Rouge, La.

VITAMINS AND THE EYE, EAR, NOSE AND THROAT: A REVIEW OF RECENT LITERATURE. ISAAC H. JONES; HAROLD S. MUCKLESTON, EUGENE R. LEWIS, WALTER P. COVELL and LELAND G. HUNNICUTT, Laryngoscope **53**:767 (Dec.) 1943.

Some astonishing cures have been attributed to vitamins in the past. The recent literature chiefly concerns scientific work and gives few clinical results of the therapeutic use of vitamins, particularly in regard to diseases of the eyes, the ears, the nose and the throat.

One recent advance is that concerning vitamin A and color blindness. At first the problem seemed a simple one, but later complexities occurred. Some results were confusing and contradictory, and other work indicated that vitamins B₂, D and C were also related to this condition.

Under the heading "Vitamins in General" the authors discuss the vitamin contents of foods and note that there is great variance in the vitamin content of a given food, depending on its preparation, cooking, source and other factors. The authors mention the valuable contributions of Fricke and Rosenberg to the subject of the vitamins. They discuss the relation of vitamins K and C to hemorrhage. The relation of vitamins to infection of the upper respiratory tract was studied by Cowan, Diehl and Baker. They concluded that in persons with an adequate diet the addition of any of the vitamins had no effect on the incidence or the severity of infections of the upper respiratory tract. The opposite is also true; that is, the lack of almost any of the vitamins, or of the other food elements essential for nutrition, will result in lowered resistance to infection. Likewise, vitamin A is closely associated with the health of the mucous membranes. Deficiency in this vitamin must be guarded against. Infection itself increases the need for vitamins. An adequate supply should be maintained during all infections.

The authors discuss the various vitamins in detail. In regard to vitamin B₁ they note that the upper limit of intake for safety is seldom reached in American diet. The development and the health of the teeth are influenced by the B complex, vitamin D and vitamin K. Palmer found that vitamin B₁ was very effective in migraine. Others found that moderate vitamin C deficiency was often encountered in medical practice. Pelner noted that there was a reduction in sensitivity to salicylates and to the sulfonamide compounds when vitamin C was administered in large doses. The tensile strength of wounds is higher in animals having a high vitamin C content.

The authors discuss the intake of foods, pointing out that vitamins are merely activators. Without the proper foods, or raw materials, the activators are useless. The importance of an adequate intake of minerals is emphasized. Intake of the proper raw materials and vitamins is particularly important for pregnant women and infants.

HITSCHLER, Philadelphia. [ARCH. OTOLARYNG.]

THE VITAMIN FACTOR IN THE ETIOPATHOGENESIS OF DYSTROPHIES. RAMIRO PAVON CABALLERO, Bol. Soc. cubana de pediat. **15**:285 (May) 1943.

This is a general dissertation on the multiple dystrophic states of infancy due to vitamin deficiency—rickets, scurvy, the syndrome of pellagra-beriberi described by Professor Castellanos and so forth—and on the importance of knowing the etiopathogenesis of each of these states for the early administration of vitamins.

KEITH, Rochester, Minn.

Hygiene; Growth and Nutrition; Public Health

HEALTH EXAMINATION FOR SCHOOL CHILDREN REQUIRED BY LAW. RAY O. DUNCAN, Illinois M. J. **86**:17 (July) 1944.

The sixty-third general assembly of Illinois passed a law which requires that all pupils of elementary and secondary schools, with certain exceptions, immediately prior to or on their entrance into the first grade, and not less frequently than every fourth year thereafter shall have physical examinations. Additional health examinations may be required when they are deemed necessary by school authorities.

Such examinations shall be made by physicians and dentists licensed to practice in the state. Cumulative records of such examinations shall be kept by the school authorities.

A pupil objecting to physical examinations on constitutional grounds shall not be required to submit himself to such examination if he presents to the board of education a statement of such objection signed by a parent or a guardian. Exempting a pupil from the physical examination does not exempt him from required participation in the program of physical education and training provided in the act.

BARBOUR, Peoria, Ill.

STUDIES ON THE DEVELOPMENT OF ARGENTINE CHILDREN. ENRIQUE C. R. BONFILS, Arch. argent. de pediat. **21**:485 (June) 1944.

The development of school children of the city of Paraná, Argentina, was studied with special regard to height, weight and thoracic expansion. Mayet's index was determined as well.

A comparison is given between children from Buenos Aires and from Paraná.

CASSORLA, Chicago.

COW'S MILK AND HEALTH LEGISLATION. MAXIMINO FERRER CARTAYA, Bol. Soc. cuba de pediat. **15**:389 (June) 1943.

The author discusses the composition, qualities, fermentations, and so forth, of whole cow's milk and names the diseases which may be transmitted by the milk. The regulations in regard to all phases of milk control are cited in detail.

KEITH, Rochester, Minn.

Prematurity and Congenital Deformities

THE CARE OF CLEFT LIP AND PALATE IN BABIES. LOUIS W. SCHULTZ, Illinois M. J. **86**:138 (Sept.) 1944.

This treatise on cleft lip and palate in babies, discussing causation, varieties, complications, time for treatment, anesthetics, surgical repair, care and prognosis, is too comprehensive and detailed for adequate abstracting.

BARBOUR, Peoria, Ill.

TWO CASES OF DOLICHOSTENOMELIA [ARACHNO-DACTYL]. T. VALLEDOR, L. VIAMONTE and LORENZO EXPÓSITO, Bol. Soc. cubana de pediat. **15**:583 (Sept.) 1943.

Two cases of arachnodactyly are reported. This condition represents a congenital dystrophy involving tissues of mesodermic origin. The main symptoms are (a) excessive length and slimness of the bones, particularly in the distal segments of the extremities; (b) underdevelopment of the muscles and lack of fat; (c) laxity of ligaments and tendons, permitting an exaggerated range of movements in the joints. There are frequently congenital abnormalities of the eyes.

KEITH, Rochester, Minn.

Newborn

ERYTHROBLASTOSIS FOETALIS: A CASE REPORT. EMANUEL B. BRANDES and HARRY R. CUSHMAN, J. Pediat. **25**:239 (Sept.) 1944.

Brandes and Cushman report a case in which erythroblastosis fetalis was successfully treated with blood transfusions.

They particularly emphasize the importance of using Rh-negative blood if adequate response is expected and show by charts the difference in hemopoietic activity which results when Rh-positive and Rh-negative bloods respectively are administered. After three transfusions of Rh-positive blood a rise of only 1,000,000 in the total red cell count was obtained, which within three days dropped 400,000. Conversely transfusion of Rh-negative blood resulted in an immediate increase of 1,500,000 red blood cells—a count which not only was maintained but was effective in stimulating hemopoiesis in the infant such that further therapy was unnecessary and complete recovery resulted.

The authors conclude that Rh-negative blood should be used in the treatment of this condition, but feel that when it is not immediately available transfusion of compatible Rh-positive blood may be of value in maintaining life until a suitable donor is obtained.

BRANDES, P. A. Surg. (R) U.S.P.H.S.

CLINICAL OBSERVATIONS IN THE TREATMENT OF EPIDEMIC DIARRHEA OF THE NEWBORN. NINA A. ANDERSON and WALDO E. NELSON, J. Pediat. **25**:319 (Oct.) 1944.

In an outbreak of epidemic diarrhea of the newborn involving 24 full term and 4 premature infants, 1 premature infant died. Among these infants, 7 were classified as critically ill, 8 as seriously ill, 8 as moderately ill and 5 as mildly ill. In all of the infants the disease developed within seven days.

Bacteriologic studies revealed a para-aerogenes type of paracolon bacillus in the stools of 9 of these infants. No specific antibodies could be demonstrated in serums collected from 7 of the infants two to four weeks after the onset of the disease.

The obstetric department was closed to new admissions, the attacked infants segregated from the exposed ones and a temporary obstetric unit for new patients established on another floor of the hospital, from which the nurses and the physicians responsible for the ill infants were excluded. Infants who had been discharged recently from the nursery were followed closely for any evidence of the disease.

The plan of treatment included substitution of a modified oral feeding for the milk feeding, subcutaneous

and intravenous administration of fluids, correction of states of acidosis by parenteral administration of alkali and oral administration of synthetic ascorbic acid and thiamine hydrochloride. Several of the infants received transfusions of blood or of plasma. All of the infants received succinylsulfathiazole orally.

Of particular importance were the detection of states of acidosis in infants many of whom did not present the classic clinical picture of acidosis and the satisfactory clinical response to attempts at correction of the acidosis either with 5 per cent solution of sodium bicarbonate given intravenously or with sixth-molar solution of sodium-lactate given subcutaneously and/or intravenously, in calculated amounts. In 50 per cent of the instances in which the infants showed abnormal manifestations the carbon dioxide-combining power of the blood was 35 volumes per cent or less. Criteria for carbon dioxide determinations included listlessness, restlessness, failure to gain weight or loss of weight, cherry red lips, hyperpnea and diarrheal stools.

The need for constant observations of the ill infants is stressed, and it is suggested that carbon dioxide determinations be obtained whenever there is evidence of increased severity of illness with or without the usual manifestations of acidosis.

ANDERSON, Philadelphia.

INFECTION IN THE NEWBORN. J. L. HENDERSON, Edinburgh M. J. 50:535 (Sept.) 1943.

The author speaks of the Honyman Gillespie lectures, given in Edinburgh, Scotland, in 1943 by Professor McNeil and Dr. Agnes MacGregor, in which the problem of infection during the first month of life was referred to. Henderson goes into greater detail as to the problem of infection in the first month of life. He states that infections rarely bring on death in the first three days or in the latter part of the first week: It is after the first week that most of the deaths are caused by infection. He cites 71 fatalities from infection from the second to the fourth week inclusive, while there were only 43 deaths from all other causes.

Efforts to prevent cross infection in maternity hospitals must deal with overcrowding of infants in nurseries, absence of barrier-nursing precautions and in many cases inadequacy of the nursing staff. The author states that the prevalence of cross infections found nowadays in hospitals, about one hundred years after the discoveries of Pasteur and Lister, is a poor tribute to the memory of these men.

NEFF, Kansas City.

Acute Contagious Diseases

CONGENITAL CATARACT AND OTHER ANOMALIES FOLLOWING GERMAN MEASLES IN THE MOTHER. ALGERNON B. REESE, Am. J. Ophth. 27:483 (May) 1944.

All 3 of the author's patients had congenital cataracts and congenital cardiac lesions. All mothers contracted German measles within the first month of pregnancy. The author asks a few pertinent questions, such as: Is the infection of the mother really German measles, and, if so, why have the congenital anomalies reported by him not been observed previously? Can any prophylactic measures be taken to prevent pregnant women from contracting German measles during the first three months of pregnancy, and should a pregnant woman who contracts an exanthem in the first three months of pregnancy have abortion performed?

STRAKOSCH, Denver. [Arch. Dermat. & Syph.]

RELATIONSHIP OF POLIOMYELITIS AND TONSILLECTOMY.

R. E. HOWARD, Ann. Otol., Rhin. & Laryng. 53:15 (March) 1944.

Howard reviews the reports of the relation between poliomyelitis and tonsillectomy. Such a relation was first suggested as early as 1910. The organism that causes poliomyelitis is a filtrable virus which may be presented on any surface of the gastrointestinal tract, from the lips to the lower part of the bowel, of a person afflicted with the disease, a convalescent patient or a carrier. It is widely distributed among normal people but manifests itself only in susceptible ones. The infection may be transferred by hands, handkerchiefs, towels and other articles recently handled by so-called carriers or by persons having the disease. It may also be spread by coughing, sneezing, loud talking or laughing. The recovery of the virus from sewage and flies in infected areas makes one believe that there are indirect methods of spread. The consensus at present is that the virus enters through the mucosa of the alimentary tract.

In his conclusions the author makes the following statements: The possibility of poliomyelitis following removal of tonsils and adenoids during July, August, September and October in nonepidemic years is minimal, but when it does occur it is serious and often of the bulbar type. The ratio is 1 in 2,000 operations. The possibility of the disease following the operation in the other eight months is nil except in Texas and California, where the season for poliomyelitis lasts from June to November, and occasionally to December. Preventive medicine as practiced now by the boards of health throughout the nation shows that during the months and years when there are epidemics of poliomyelitis, operations on the nose and the throat should be avoided whenever possible.

M. V. MILLER, Philadelphia [Arch. Otolaryng.]

COMBINED IMMUNIZATION AGAINST PERTUSSIS, DIPHTHERIA AND TETANUS. PAUL M. HAMILTON and E. G. KNOUF, J. Pediat. 25:236 (Sept.) 1944.

Sixty-four normal infants between the ages of 12 and 18 months were given a combined mixture of antigens to induce immunity to diphtheria, whooping cough and tetanus by one series of inoculations. The fluid toxoids of diphtheria and tetanus were produced, tested, sterilized and titrated for dosage in the usual way; to this mixture of the two toxoids pertussis phase I vaccine was added to yield 40,000,000 organisms per cubic centimeter. The doses were 0.5, 1 and 1 cc., given subcutaneously at intervals of one month. Three months later samples of blood were tested for their agglutinating titer against the pertussis organism and for their content of diphtheria and tetanus antitoxins.

Results showed as consistent and as high a degree of immunity as is expected when each procedure is done separately. Reactions to inoculations were usually entirely absent, and in no case were they troublesome.

It is suggested that such a simplified procedure, with its saving of time for doctors and its appeal to parents, may result in more nearly universal immunization of infants.

HAMILTON, San Marino, Calif.

RUBELLA EARLY IN PREGNANCY CAUSING CONGENITAL MALFORMATIONS OF EYES AND HEART. CARL A. ERICKSON, J. Pediat. 25:281 (Oct.) 1944.

The author reports the cases of 11 infants with congenital cataracts, 9 of whom had noncyanotic heart disease as well, whose mothers had rubella during the

first few months of pregnancy. The fact that embryonic tissues are very susceptible to virus infections makes it seem plausible that the mothers had a mild systemic infection due to a virus, which attacked the growing fetus and injured structures which were in early stages of development, namely, the lens and the heart. Other infections due to viruses have at times been incriminated, and other malformations are occasionally produced.

AUTHOR'S SUMMARY.

PERTUSSIS: BACTERIOLOGIC AND AGGLUTINATION STUDIES. JESSE G. M. BULLOWA, LILLIAN BUXBAUM and IRVING E. SCHEINBLUM, *J. Pediat.* **25**: 299 (Oct.) 1944.

Early diagnosis of pertussis is desirable both from the epidemiologic standpoint and for treatment, and yet it is especially difficult. The Chevitz-Meyer cough plate method for obtaining cultures has been used since 1916 by many workers, with varying results. In 1940 Bradford and Slavin adopted the nasopharyngeal swab for culturing *Hemophilus pertussis* from patients with whooping cough and had much greater success. Patients' agglutinin titers have also been determined and an effort made to adapt this procedure to diagnostic purposes, but many conflicting reports are found in the literature. In an effort to evaluate the laboratory methods for the diagnosis of pertussis cough plates, nasopharyngeal swabs and mucus obtained by laryngeal suction were taken for cultures at the same time as blood for determining the agglutinin titer from 53 patients showing clinical evidence of whooping cough.

The "cough plate" cultures were obtained by holding the Petri dish containing the medium 6 inches (15 cm.) from the patient's mouth for from thirty to forty coughs during a paroxysm. The nasopharyngeal swabs were taken by passing a straight wire with a sterile cotton tip through the nares to the posterior pharyngeal wall. A rubber catheter attached to a suction bulb was used to aspirate mucus from the larynx.

A modification of the Bordet-Gengou medium with proteose peptone and nicotinic acid was used for culturing all specimens. The nasopharyngeal swabs were rotated on the corner of one plate and then by the use of a straight wire were streaked through the corner and serially onto a second plate. The laryngeal secretions were treated in a like manner except that three plates were used. In this manner individual colonies of *H. pertussis*, free from secondary microorganisms, were obtained. Typical colonies were identified by stained smears and were confirmed by agglutination.

Agglutination titers were determined by the slide method (Mishulow's modification of the Welsch-Stuart test). Varying amounts of patient's serum and a standard antigen (Lilly) were used.

The 53 patients studied were young children, 28 being under 1 year, 18 between 1 and 3 years and 7 between 3 and 6 years of age. The duration of illness ranged from three to forty-four days at the time of the culture and the agglutination test. *H. pertussis* was isolated from 40 (75.5 per cent) of the patients by one or more of the methods. Specimens obtained by nasopharyngeal swabs yielded the greatest number of positive cultures (87.5 per cent), and laryngeal suction yielded more positive cultures than cough plates in every age group and in every week of illness.

However, the suction method of obtaining specimens was found to be cumbersome, and therefore it is not considered desirable as a routine procedure. Cough plates in combination with nasopharyngeal swabs were found to yield the greatest number of positive cultures. There was direct correlation between the duration of

illness and the number of positive cultures obtained; 83.3 per cent during the first ten days of illness and 60 per cent during the fourth week of illness.

There was little correlation between results of cultures and agglutination titers. Of the 38 patients who had positive cultures only 9 showed the presence of agglutinins, and of the 12 patients who had negative cultures 3 had demonstrable agglutinins. Although the age of the patients seemed to have no bearing on the production of agglutinins, the duration of illness played a significant role, as only 3 patients had detectable agglutinins before the second week of illness.

BULLOWA, New York.

ACUTE POLIOMYELITIS DURING PREGNANCY. ALFRED FLAUM, *Nord. med.* **18**:563 (April 3) 1943.

A 27 year old woman in her first pregnancy fell ill two days before delivery with typical signs of poliomyelitis and died a few days later of respiratory paralysis. The infant was healthy and remained so.

WALLGREN, Stockholm, Sweden.

POLIOMYELITIS IN PREGNANCY. ÅKE NETTELBLAD, *Nord. med.* **18**:657 (April 17) 1943.

This is a report of 6 cases of poliomyelitis involving pregnant women. One of the women died after cesarean section, performed in order to facilitate the breathing, which was impaired through paralysis of the diaphragm. The infant died. Another infant displayed a certain degree of atrophy of the muscles, which was thought to be due to intrauterine poliomyelitis. In the 4 other cases the children were normal and had suffered no harm from the poliomyelitis which their mothers had during their fetal period.

WALLGREN, Stockholm, Sweden.

CASE OF PAROTIC MENINGITIS WITHOUT SIGNS OF PAROTITIS. ADOLPH H. MEYER, *Nord. med. (Höspitalstid.)* **17**:257 (Feb. 13) 1943.

A 6 month old boy had convulsions and fever. The spinal fluid contained many cells, of which 70 per cent were lymphocytes and 30 per cent larger mononuclear cells. The sugar content of the urine was 54 per hundred cubic centimeters. The patient became afebrile after one week and was discharged healthy. The salivary glands were not enlarged and showed no tenderness. The boy was the fifth of 5 siblings, of whom 3 had had parotitis.

WALLGREN, Stockholm, Sweden.

A CLINICAL SYNDROME IN CHILDREN RESEMBLING RHEUMATIC FEVER. ALBERT D. KAISER, *New York State J. Med.* **43**:1937 (Oct. 15) 1943.

This is part of a symposium on rheumatic fever. In acute rheumatic fever in children the heart is probably always involved, and the discovery of some type of cardiac involvement is necessary for a correct diagnosis. Kaiser reports a group of 200 cases of a condition that resembled rheumatic fever except that there were no murmurs. The electrocardiograms were normal, and there was little change in the sedimentation rate. He believes that these represent a separate clinical syndrome and should not be considered rheumatism. The condition has much the same pattern as rheumatic fever, with pain in the knees, legs and thighs, fatigue, pallor, loss of appetite, slight rise in temperature, sore throat, headache and epistaxis. The patients respond to salicylates and to rest in bed. There is a familial tendency, and there may be recurrences.

AIKMAN, Rochester, N. Y.

PREVENTION OF RHEUMATIC RECURRENCES. ANN G. KUTTNER, New York State J. Med. **45**:1941 (Oct. 15) 1943.

This is part of a symposium on rheumatic fever.

Convalescent or sanatorium care provides rest in bed and increases the child's resistance. Vitamin therapy has shown no appreciable results in preventing rheumatism. Changes in climate reduce the number of recurrences, but the results are not impressive. Desensitization has not been particularly satisfactory. Salicylates used prophylactically are of value. Kuttner's studies show that it is most important to reduce the incidence of streptococcal infections of the upper respiratory tract. This is best done by the use of sulfanilamide—1 or 2 Gm. daily between attacks. She reports more toxic reactions than are shown by Coburn, Thomas and others.

AIKMAN, Rochester, N. Y.

INFECTION WITH STRONGYLOIDES IN CHILDREN IN BAHIA. ELIEZER AUDIFACE, *Pediat. puericult. Bahia* **13**:39 (Sept.) 1943.

Strongyloides stercoralis parasitism is common in Bahia, and in every child with chronic diarrhea a search for the worms should be made. Medication is not very efficacious; gentian violet is the most satisfactory agent, although it is poorly borne by some and the results are frequently disappointing. When it is not tolerated by mouth, 15 cc. of a 2 per cent solution may be given by rectum. In addition to profound cachexia, there are severe hypochromic anemia and constant eosinophilia. All organs of the body may be attacked by this parasite.

DWYER, Kansas City, Mo.

SULFANILAMIDE IN THE TREATMENT OF ACUTE BACILLARY DYSENTERY IN CHILDREN. K. T. CHEN and I. L. TANG, *Chinese M. J.* **61**:110 (April-June) 1943.

The authors state that the most common infection during the summer months in China is bacillary dysentery, although typhoid is nearly as frequent. Between them the two diseases fill nearly all of the beds in the children's wards. The patients' stay in the hospital averages about three weeks when there is no specific or effective therapy for the bacillary dysentery, and many young children die of the disease each year.

Only patients who are severely infected or acutely ill are admitted to the hospital. Treatment with sulfonamide compounds is now the therapy of choice, the daily dose being 100 to 150 mg. per kilogram of body weight; a third or a quarter of the total twenty-four hour allowance is given as the initial dose each day. Sodium bicarbonate is given with the sulfanilamide. Improvement usually occurs by the fourth day, at which time the dose is reduced; the medication is continued for as many as five days. Of 52 patients thus treated (2 of whom received sulfathiazole instead of sulfanilamide) 2 showed toxic effects, which consisted of hematuria in 1 instance and pneumonia, hemolytic anemia and death in the other. Of 25 patients with severe infections 3 died.

The results of the treatment with sulfonamide compounds were definitely good. In most cases an improvement in the general condition took place within twenty-four hours. Subsidence of the fever was the second evidence of improvement in order of frequency and of appearance; concurrently the stools became reduced in number. There has been a definite shortening in the stay in the hospital since this treatment has been used.

NEFF, Kansas City, Mo.

Chronic Infectious Diseases

TUBERCULOUS ALLERGY. ALBERTO CHATTAS, *Arch. argent. de pediat.* **21**:504 (June) 1944.

A historical survey of tuberculin as a diagnostic aid is given. The ordinary technics for tuberculin tests, such as those for the von Pirquet, Mantoux, Moro and patch tests, are described and critically analyzed.

Theoretic considerations about tuberculous allergy, anergy and preallergy are given, with especial mention of temporary and constitutional energy, atergy, latent allergy, etc.

The clinical value of the tuberculin test is finally emphasized, along with a critical study of its limitations as a specific therapeutic agent.

CASSORLA, Chicago.

SYMPOSIUM ON THE PRIMARY INFECTION OF TUBERCULOSIS AND CHILDEOOD: INTRODUCTION. GUSTAVO CARDELLE, *Arch. de med. inf.* **13**:73 (April-June) 1944.

This entire issue of the journal is devoted to infantile tuberculosis. In the introductory article the various classifications of the disease are discussed.

SANFORD, Chicago.

SYMPOSIUM ON TUBERCULOSIS: PATHOLOGY AND DIAGNOSIS. GUSTAVO CARDELLE, *Arch. de med. inf.* **13**:84 (April-June) 1944.

This excellent article should be read in full. An interesting point is the frequency of positive reactions to tuberculin tests in the Children's Hospital Habana, Cuba: 3.3 per cent in infants up to 3 months of age, 8.9 per cent in infants 4 to 6 months of age, 12.8 per cent in infants 7 to 9 months of age, 12.9 per cent in infants 10 to 12 months of age and 14.3 per cent in infants 13 to 24 months of age. In the author's series the mortality from a primary infection was as follows: 1 day to 12 months, 45 per cent; 13 months to 2 years, 38.7 per cent; 3 years to 7 years, 4.8 per cent, and 7 to 12 years, 0 per cent. In the diagnosis, the total leukocyte count is of interest. It was under 10,000 in only 16 instances, while it was between 11 and 20,000 in 48 instances, between 21 and 30,000 in 22 instances, between 31 and 40,000 in 13 instances and over 40,000 in 3.

SANFORD, Chicago.

SYMPOSIUM ON TUBERCULOSIS: CLINICAL RADIOLOGY. RAÚL PEREIRAS and B. SÁNCHEZ SANTIAGO, *Arch. de med. inf.* **13**:124 (April-June) 1944.

Twenty-two excellent roentgenograms are shown, and the related cases are discussed. This article should be read in full.

SANFORD, Chicago.

SYMPOSIUM ON TUBERCULOSIS: COMPLICATIONS. GUSTAVO GARCÍA MONTES, *Arch. de med. inf.* **13**:152 (April-June) 1944.

The complications discussed are atelectasis and obstructive emphysema, bronchiectasis and spontaneous pneumothorax. These conditions are illustrated by roentgenograms and clinical studies.

SANFORD, Chicago.

SYMPOSIUM ON TUBERCULOSIS: ANATOMIC PATHOLOGY. JUAN A. JIMÉNEZ, *Arch. de med. inf.* **13**:161 (April-June) 1944.

Photomicrographs and photographs of gross specimens are shown in illustration of the various types

of lesions. An excellent schematic drawing is given, showing the mode of formation of the various lesions.

SANFORD, Chicago.

SYMPOSIUM ON TUBERCULOSIS: PROPHYLAXIS AND TREATMENT. ROBERTO VALDÉS DÍAZ, Arch. de med. inf. **13**:176 (April-June) 1944.

The author recommends vaccination with BCG as a form of prophylaxis and outlines the method in use in Cuba. The principles of active treatment can be grouped under three major headings: (1) protection against future infections; (2) absolute rest for the organism; (3) marshaling the best conditions as a defense against the infection.

SANFORD, Chicago.

FEEDING OF THE TUBERCULOUS CHILD. SANTIAGO BERNARDINO NAVARRO, Bol. Soc. cubana de pediat. **15**:303 (May) 1943.

The author starts his article with a general consideration of nutritional factors (protein, carbohydrates, fats, minerals and vitamins) and their respective sources. Referring, then, to the feeding of the tuberculous child, he states that the child must not be overfed and must eat what he is able to digest, although his extra needs for minerals and fats because of his growth must always be considered. Other factors to consider are fever, degree of infection, malnutrition and climate.

The presence of diarrhea or of constipation may necessitate special diets, and secondary infections, because of their influence on appetite, must receive adequate treatment. The diet must be pleasant to the child, must be rich in proteins and fats and must fill caloric requirements. For an infant breast milk is the first choice and cow's milk, if tolerated, the second.

For a critically ill patient, for example, a child with meningitis, feeding by tube is necessary.

KEITH, Rochester, Minn.

THE HYGIENE OF THE TUBERCULOUS CHILD. EVA PAGOLA, Bol. Soc. cubana de pediat. **15**:429 (June) 1943.

This is a discussion for nurses of the general principles underlying the care of patients with tuberculosis and the prevention of the spread of infection. "The prophylaxis of tuberculosis is above all a problem of education."

KEITH, Rochester, Minn.

PRIMARY CERVICAL TUBERCULOSIS IN THE CHILD—"MACROADENOPATHY" T. VALLEDOR, Bol. Soc. cubana de pediat. **15**:455 (July) 1943.

Nine cases of primary cervical tuberculosis in small children are reported. Seven of the children were 3 years of age or younger; 5 were white and 4 Negro. In 7 cases a member of the family or some other person was the source of infection, 1 was considered due to contaminated milk and in 1 no source could be found. In 1 instance a cutaneous lesion was present on one cheek. In 8 cases the adenitis involved all the cervical lymph nodes. Consecutive involvement of the mediastinal lymph nodes was noted in 4 instances—in 1 the involvement was contemporaneous. The reactions to the Mantoux test were strongly positive and the erythrocyte sedimentation rate accelerated in the entire series. In 5 cases biopsy confirmed the diagnosis. Patients were observed from a few months to five years. Treatment was conservative, without surgical intervention. All patients were given iodine by mouth. No lesions in the lungs were observed at any time, and the progress of all the patients was good. The

cases are reported in detail with illustrations, roentgenograms, photographs of patients and specimens.

KEITH, Rochester, Minn.

EPIDEMIOLOGIC INVESTIGATION OF TUBERCULOSIS. T. VALLEDOR, A. FERIA, J. CORNEJO and A. FERNÁNDEZ BALTRÓNS, Bol. Soc. cubana de pediat. **15**:561 (Aug.) 1943.

This is a report of the results of tuberculin tests on children of various ages attending the Hospital Mercedes in Habana, Cuba. The percentage of positive reactions in children from birth to the age of 13 years was 23.03 during the years 1940 and 1941. There were approximately twice as many positive reactions among Negro infants as among white infants, a circumstance which probably reflects poor hygienic conditions among the Negro families.

KEITH, Rochester, Minn.

COEXISTENCE OF PULMONARY SUPPURATION AND TUBERCULOSIS IN CHILDREN. RAUL MATTE L. and SERGIO IBÁÑEZ Q., Rev. chilena de pediat. **14**:887 (Dec.) 1943.

The authors point out that often only careful, prolonged study can differentiate between pyogenic pulmonary abscess and tuberculous cavitation; suppurative pulmonary disease may often activate healing tuberculosis. Five illustrative cases are presented.

PLATOU, New Orleans.

BACILLARY DYSENTERY IN CHILDHOOD. ALFONSO COSTA and HERNAN ROMERO, Rev. chilena de pediat. **14**:905 (Dec.) 1943.

Results of 1,622 stool cultures taken from 618 sick infants are analyzed. One hundred and thirty-two of the infants had clinical enterocolitis. In 29.1 per cent of the 132 cases dysentery organisms were isolated on lactose agar and were further identified by agglutination reactions; Shiga's type was found 8 times; Flexner's 25 times and Sonne's 6 times. From 488 sick infants without enterocolitis (controls), only 2 positive cultures were secured. Clinical features influencing the course of the dysenteries are discussed.

PLATOU, New Orleans.

Diseases of Blood, Heart and Blood Vessels and Spleen

INCREASED RED BLOOD CELL FRAGILITY AFTER FAT INGESTION. JOAN LONGINI and VICTOR JOHNSON, Am. J. Physiol. **140**:349 (Dec.) 1943.

The statement that ingested fat may be injurious to red blood cells has appeared in medical literature. The authors set out to investigate whether this might be true. Their studies were made with dogs. They found that after ingestion of fat an agent which increases the fragility of red blood cells is present in dog's serum. Neutral fat is not this agent. Free fatty acids and soaps reaching the blood stream by way of the lymphatics are probably responsible for the effect. Ingestion of carbohydrates and proteins does not increase the fragility of the red cells. On the contrary, meals rich in these substances produce serum which may actually protect red cells from water hemolysis. The suggestion is made that those physiologic mechanisms which delay the absorption of fat and its entrance into the blood stream are probably significant in the prevention of anemia.

STOESSER, Minneapolis.

COR BILOCULARE. FRED R. SHECHTER and DAVID R. MERANZE, *J. Pediat.* **25**:150 (Aug.) 1944.

A case of cor biloculare is reported involving a girl born at term who lived twenty-three days. The important anatomic changes noted at autopsy were displacement of the heart into the right side of the thoracic cavity, a cor biloculare with dilatation, particularly of the ventricle, a hypoplastic systemic aorta with virtual functional atresia, a persistent and prominent ductus arteriosus and diffuse ventricular endocardial fibrosis. No other somatic anomalies were present. Clinically, cyanosis was the outstanding symptom. The infant died of cardiac failure.

AUTHORS' SUMMARY.

PERIARTERITIS NODOSA. EDWIN PAUL SCOTT and C. C. ROTONDO, *J. Pediat.* **25**:306 (Oct.) 1944.

The authors report 2 cases of periarteritis nodosa in children in which death was sudden. Periarteritis nodosa of the coronary arteries was demonstrated at autopsy in both patients; in 1 there was fatal intrapericardial hemorrhage due to rupture of an aneurysm resulting in tamponade, and in the other the pathologic changes were so extensive that rupture of the coronary vessels seemed imminent.

SCOTT, Louisville, Ky.

ABNORMAL ORIGIN OF THE LEFT CORONARY ARTERY WITH EXTENSIVE CARDIAC CHANGES IN A FEMALE CHILD THIRTEEN MONTHS OLD. FREDERICK PROESCHER and FRANZ W. BAUMANN, *J. Pediat.* **25**:344 (Oct.) 1944.

The authors report the case of a 13-month old girl with so-called chronic bronchitis in whose left lung there had developed what would appear to be an acute pneumonic process. The infant was hospitalized twenty-four hours after onset of this acute condition and died shortly thereafter. Laboratory tests had not been completed. Autopsy revealed that the left coronary artery originated from the pulmonary artery instead of from the aorta. The heart was greatly enlarged and showed numerous degenerative changes with necrosis and calcification of muscle fibers. So-called embryonic sinusoids, previously seen by other authors only in the myocardium, were seen not only in that structure but in the pericardium. The authors' patient is the oldest infant in whom origin of the left coronary artery from the pulmonary artery has been reported. It appears that some patients do not present the clinical history which, according to a previous reviewer, suggests the presence of this anomaly. Attention is called to the observation that this condition appears to be more frequent in female infants. Photomicrographs accompany the article.

AUTHORS' SUMMARY.

A CASE OF INTERAURICULAR COMMUNICATION. ALFREDO E. LAEGUA and JUAN C. CAPRILE, *Arch. argent. de pediat.* **21**:533 (June) 1944.

A case of a 13 year old girl presenting a form of cardiopathy which after extensive consideration was classified as interauricular communication is reported.

This condition is a variety of the Abbott type of "cardiopathy with late cyanosis." Comments on the diagnostic importance of roentgen films, angiocardioraphy and electrocardiography are given.

CASSORLA, Chicago.

Diseases of Nose, Throat and Ear

STUTTERING: I: A CRITICAL REVIEW AND EVALUATION OF BIOCHEMICAL INVESTIGATIONS. HARRIS HILL, *J. Speech Disorders* **9**:245, 1944.

This is a review of modern literature on the biochemistry of stuttering. No corroborative findings have been made in regard to a possible biochemical cause of stuttering. The author believes that if such findings were made they could be demonstrated to be the result rather than the cause of stuttering.

PALMER, Wichita, Kan.

AUDITORY MEMORY SPAN FOR MEANINGLESS SYLLABLES. HELEN HULICK BEEBE, *J. Speech Disorders* **9**:273, 1944.

Observations on a group of 207 children ranging in age from 4 years to 8 years 5 months, including 86 boys and 121 girls, were compared with the findings of Weiss and Froeschels in German children. The average values for the auditory memory span fell below those for the German-speaking children. The small number of subjects, however, does not make for complete confirmation of these results.

PALMER, Wichita, Kan.

DIAGNOSIS AND TREATMENT OF SINUSITIS IN CHILDREN. D. E. STAUNTON WISHART, *Laryngoscope* **54**:97 (March) 1944.

Sinusitis is frequent in children, occurring in perhaps 30 per cent.

Much more should be known of the anatomy and the physiology of the nose. The author shows that the bony structure and the mucosa of the inferior turbinate are of a little known and very special design. He describes it from the point of view of anatomy. He also describes the ostia of the sinuses. They can be compared to manholes almost completely filled with hoses (nerves, arteries, veins). Injury to a sinist ostium may seriously damage the sinus. The middle turbinate region is the most important from the point of view of the etiology of sinusitis, for most of the sinuses open into this area.

In the diagnosis of sinusitis a careful history is important. The symptoms include stuffy nose, nasal discharge, nasopharyngitis, protracted fever, cough, post-nasal drip (only older children notice it), headache (rare up to the age of 6), pain and impairment of the sense of smell (indicative of ethmoiditis).

The histopathologic changes in disease of the sinuses are described. The importance of preventing the onset of chronic sinusitis is stressed.

Careful shrinking, transillumination and nasopharyngoscopic and roentgen examinations should be carried out in order to establish a diagnosis. Radiopaque substances are often of value.

Sinusitis must be differentiated from allergic rhinitis. Many of the symptoms and signs are not reliable for differential diagnosis. Two things are reliable, however: (1) the impossibility of shrinking the nasal mucosa of the allergic patient with cocaine, epinephrine or ephedrine and (2) the appearance of an excessive number of eosinophils in the nasal secretions and the sputum in allergy.

Treatment is discussed. Splashing the face with cold water and using the steam kettle often improve the physiologic function. Crying and sneezing are aids in getting rid of nasal secretion. The use of faintly acid nose drops is recommended. Stagnant, thick mucin promotes bacterial growth and should be removed.

Irrigations with warm saline solutions help remove it. They must be given properly (the face downward). The lateral head low position is also good. With it the middle meatus can be shrunk and cleared. Washing of the maxillary sinus by a needle puncture under the middle turbinate is recommended, while washing via a natural ostium is condemned.

The author does not treat children's sinuses by displacement. The child is afraid, and its confidence is lost. Furthermore, uninfected sinuses may become infected. Tampons or packs are condemned. Short wave and roentgen treatment have not proved beneficial. The results of treatment with sulfonamide compounds are encouraging but not conclusive. The protracted use of sulfonamide compounds is not advised.

The author disapproves in general of surgical operation on the sinuses in children. Excellent results were achieved by conservative therapy at the Hospital for Sick Children, in Toronto, Canada. In each case the disease must be first properly diagnosed and then treated conservatively. The surgeon must perform only measures that are needed and no more. He must handle the postoperative care himself. The purpose of surgical intervention is to restore the nose and sinuses to a good physiologic condition.

The removal of the anterior third of the middle turbinate is often of great value, particularly if it blocks the middle meatus. Better drainage results.

The inferior turbinate has great functional value and should not be disturbed. Removal, cauterization and coagulation of this structure should not be performed.

Major surgical procedures have their place but should be avoided if possible.

HITSCHLER, Philadelphia. [ARCH. OTOLARYNG.]

TREATMENT OF EXTERNAL OTITIS: I. LOCAL SULFONAMIDE THERAPY. BEN H. SENTURIA, Laryngoscope **54:277** (June) 1944.

External otitis is an important disease in the warmer climates. The causative organisms are probably a mixture of both bacteria and fungi. The bacteria may be various kinds of streptococci, staphylococci, diphtheroids and *Bacillus pyocyaneus*. The fungi may be spores of *Penicillium*, *Aspergillus* and *Monilia*. They are saprophytic fungi. True pathogenic fungi are rarely found.

Fungi need carbohydrates for their growth. They flourish in ear wax. Moisture is necessary for them to obtain close contact with their source of energy. Toxins are produced by the growth of the fungi. These irritate the surface epithelium. The bacteria present then invade this irritated epithelium.

Signs and symptoms vary from a feeling of blockage, dryness, itching, scaling, or slight tenderness on manipulation of the external canal to varying amounts of pain, edema of the wall of the canal, glandular swelling and slight fever.

In treatment, a mixture of sulfanilamide, sulfathiazole and zinc peroxide powders (4:2:2) was found most efficacious. It was blown into the ear after this had been cleaned mechanically and with hydrogen peroxide.

The patients were seen daily for several days. Sedation was given as necessary. As the condition improved, irrigation with sodium bicarbonate solution was used to wash out all the accumulated debris and powder. Irrigation was done only when the edema and the tenderness had subsided enough to permit drying of the canal afterward. This was followed with instillation of alcohol. In several minutes this was allowed to run out. The residuum in the canal soon evaporated.

Powder was then reapplied and left in for a week. The patient was cautioned against getting water into or about the ears, and swimming was forbidden.

In all the cases of acute infection the condition responded well, only 1 patient in 33 requiring more than seven days for a complete cure. No recurrences were observed. In other cases, as a control, treatment was by dry wipes, alcohol and sulfanilamide in alcohol. In these the condition did not respond so quickly, and in some recurrences were noted. Auditory acuity was unaffected.

HITSCHLER, Philadelphia. [ARCH. OTOLARYNG.]

RADIATION THERAPY OF LYMPHOID TISSUE IN THE NASOPHARYNX AND PHARYNX. HOWARD HICKS ASHBURY, Radiology **43:250** (Sept.) 1944.

Ashbury reports the results he obtained by treating lymphoid tissue in the nasopharynx and the pharynx with high voltage roentgen therapy. He noted marked improvement in cases of conduction deafness, obstruction of the ostiums and infection when the conditions were due to lymphoid tissue. Five pairs of treatments were given over a period of thirty days. The less responsive patients were ultimately treated by applying radium directly to the lymphoid tissue (75 mg. per hour). One hundred and fifty-seven patients were treated, most of whom were in the first decade of life.

ANSPACH, Chicago.

AN ELECTROENCEPHALOGRAPHIC STUDY ON THE MOMENT OF STUTTERING. NORMAN WILLIAM FREESTONE, Speech Monogr. **9:28**, 1942.

The author reviews all previous studies of the same problem, showing that there is no general agreement in their conclusions. Twenty normal speakers and 20 stutterers, chosen without regard for handedness, were studied by means of a Gras electroencephalograph as to left and right frontal areas 1 to 6, left and right lower motor areas 2 to 5, left and right occipital areas 3 to 4 and left and right upper motor areas 7 to 8. The author does not report the sex distribution. Many of the previous findings failed to be confirmed. The brain potentials of stutterers are statistically different from those of normal persons in many areas.

The following general conclusion is reached: Psychologic stimuli must impinge on certain basic neurologic differences before stuttering can result. These differences are due to a lack of heightened foci of cerebral activity, a condition which is akin to reduced consciousness.

The following specific conclusions are reached: 1. Stutterers are neurologically differentiated from normal persons. 2. The proper stimulation of the neurologic differences forces stutterers to function in a relative state of reduced consciousness. 3. States of reduced consciousness, seen as a lack of heightened foci of cerebral activity, militate against the establishment of a dominant speech gradient. 4. The Travis hypothesis of lack of a speech gradient for stutterers is at least partially supported.

PALMER, Wichita, Kan.

A COMPARATIVE ANALYSIS OF THE RESULTS OF TESTING INDIVIDUAL HEARING AIDS IN A SCHOOL FOR THE DEAF. JEAN UTLEY and MARION GOEBEL, Speech Monogr. **10:40**, 1943.

Twenty-one children from the intermediate and advanced departments of the South Carolina School for the Deaf, 14 girls and 7 boys with ages ranging from 11 to 20, with 15 congenitally deaf patients, were studied by various methods of testing audiometric results

Various hearing aids were used in order that their effectiveness might be checked. The aids are not identified in the publication. One aid was of no benefit; 1 aided the group about 14 per cent; and 1 aided about 7 per cent. Some persons who could be aided by none of the devices were helped when the loud speaker system was used. In 1 case, 1 hearing aid apparently actually decreased the ability to hear of the child who was wearing it. The general conclusion is that several aids should be tried on any severely deaf child with the use of the pure tone audiometer.

PALMER, Wichita, Kan.

Diseases of Lungs, Pleura and Mediastinum

CHYLOTHORAX IN INFANCY. GILBERT B. FORBES, J. *Pediat.* 25:191 (Sept.) 1944.

An instance of bilateral spontaneous chylothorax in a 6 week old girl is described. Symptoms began at about 1 month of age and consisted of intermittent dyspnea and cyanosis. Diagnosis was made by the characteristic gross appearance and a detailed chemical analysis of the chylous fluid. There was no ascites, and the urine was normal at all times. During a two month hospital course, a total of 5,300 cc. of chyle was removed from the pleural cavities, thoracentesis being performed whenever respiratory symptoms warranted it: This was necessary on the average every thirty-six hours. The chyle contained 2.8 per cent protein and 0.4 to 1.2 per cent fat. Body protein and stores of fat could easily be depleted by the withdrawal of these large amounts; so it was necessary to combat malnutrition by feedings high in caloric value, numerous transfusions of plasma and of whole blood and several intravenous injections of the patient's own chyle. No reactions were observed after the latter procedure.

It was found that when large amounts of vitamins A and D were fed orally these substances rapidly appeared in the chyle in appreciable quantities. However, beta carotene did not appear in the chyle after oral ingestion.

After two months in the hospital the patient died from bronchopneumonia and a tension pneumothorax. At autopsy the thoracic duct could not be demonstrated, nor were there any lesions in the mediastinum which could possibly have obstructed it. With the exception of an unusual degree of insular hyperplasia of the pancreas, the remaining organs were normal. FORBES.

A CASE OF CHYLOTHORAX IN A TWO WEEK OLD INFANT, WITH SPONTANEOUS RECOVERY. MORRIS WESSEL, J. *Pediat.* 25:201 (Sept.) 1944.

A case of chylothorax in a 2 week old infant, with spontaneous recovery, is presented.

The infant, who had been born at term by a spontaneous delivery, was admitted to the Babies Hospital on the fourteenth day of life with cyanosis as the chief complaint and with labored respiration of twenty-four hours' duration. There was no history of a neonatal pathologic condition, trauma, convulsion, vomiting, infection of the upper respiratory tract or contagious exposure.

Physical examination presented a desperately sick infant, afebrile, who had acute respiratory distress with associated cyanosis. Immediate fluoroscopy revealed a dense shadow in the right side of the thorax, with marked mediastinal shift to the left. Thoracentesis in the right side of the thorax just below the angle of the scapula yielded 200 cc. of creamy yellowish fluid. Culture of the fluid proved sterile. Physical examination

of the infant after aspiration showed him to be essentially normal. A diagnosis of chylothorax, cause unknown, was made.

Twelve additional aspirations were performed over a thirteen day period in order to relieve respiratory distress. Amounts between 55 and 120 cc. were obtained on the various occasions. Seven months have passed since the last aspiration, and there have been no clinical or roentgenographic signs of reaccumulation of fluid. The infant was maintained on a dietary formula high in protein and low in fat, with added vitamin concentrates.

Chemical studies on the variation of composition of the chylous fluid in relation to changes in dietary intake are reported. There is also presented a review of relevant literature.

WESSEL, New York.

OBSTRUCTIVE EMPHYSEMA DUE TO TUBERCULOUS MEDIASTINAL LYMPH GLANDS. L. G. PRAY, J. *Pediat.* 25:253 (Sept.) 1944.

A report is presented of a 4½ month old infant with obstructive emphysema of the left lung as a result of tuberculous mediastinal glands. Physical examination and roentgenographic studies revealed changes typical of that condition. Bronchoscopy showed external pressure compressing the left main bronchus. Tracheotomy was necessary after bronchoscopy because of laryngeal obstruction. The infant died on the third day in the hospital. At autopsy there were large tracheobronchial lymph glands in the left hilar region obstructing the left main bronchus. Microscopic examination of these glands revealed typical tuberculous tissue.

PRAY, Fargo, N. D.

THE ROENTGENOLOGIC FEATURES OF MEDIASTINAL TUMORS. LAWRENCE L. ROBBINS, *Radiology* 43:115 (Aug.) 1944.

Robbins describes and publishes roentgenograms of the chests of patients selected from 44 having proved mediastinal tumors at the Massachusetts General Hospital. Fifteen bronchogenic cysts were encountered. Their most important roentgenographic feature was a smooth, round or ovoid shadow arising anywhere within the mediastinum. Its discovery was usually accidental. All of 7 dermoid cysts were in the anterior mediastinum, only 1 being in the upper portion. The contour usually was slightly irregular. Some showed calcification in their walls. All of the teratomas (3) were located in the anterior mediastinum. Two showed slight lobulation of outline, and 1 was smooth. All were accompanied by fluid in the pleural cavity. Of 14 tumors of neurogenic origin, 9 arose in the posterior mediastinum and 5 in the anterior mediastinum. The exact nerve from which the tumor originated was difficult to determine. Only 1 tumor proved to be malignant. It was located in the right side of the middle part of the chest and was thought from its appearance to be benign. While certain diagnostic features have been demonstrated, no exact differentiation of tumors of the mediastinum was possible to the author.

ANSPACH, Chicago.

A STATISTICAL ANALYSIS OF 100,000 EXAMINATIONS OF THE CHEST BY THE PHOTOROENTGEN METHOD. PETEA ZANCA AND FEDERICK K. HERPEL, *Radiology* 43:122 (Aug.) 1944.

The authors' experience with the photoroentgen method, using stereoscopic 4 by 10 inch (41 by 56 cm.) films, has convinced them that the use of this

smaller film is practical. These smaller single-coated films are considered better in definition than the usual 14 by 17 inch (36 by 43 cm.) single film of the chest. They are recommended because of low cost and ease of handling and processing and because they cause minimum eye strain and fatigue.

In this statistical survey, 100,000 consecutive examinations of the chests of selectees were made, using this new apparatus. Two and sixty-one hundredths of the subjects were found to have lesions of the chest.

AUSPACH, Chicago.

SIX CASES OF SPONTANEOUS VALVULAR PYOPNEUMOTHORAX. JOSÉ MARIA PELLIZA, Arch. argent. de pediat. **21**:518 (June) 1944.

The author reports 6 cases of spontaneous valvular pyopneumothorax. The importance of a correct diagnosis for better management of the patient is stressed.

Pleural tap is usually not advisable and, if necessary, should be preceded by the making of anteroposterior and lateral roentgenograms.

Pleurotomy with continuous drainage is the best treatment.

CASSORLA, Chicago.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

LONG STANDING FEVER DUE TO REGIONAL ILEOCOLITIS. P. H. SPRAGUE, W. S. ANDERSON and T. R. AARON, Am. J. Digest. Dis. **11**:295 (Sept.) 1944.

Two months after having an inflammatory process in the right knee, which apparently responded rapidly to administration of salicylates, the patient, a 15 year old girl, had what was thought to be a polyarticular type of rheumatism. There was moderate anemia, but except for tachycardia, the heart seemed normal. The Mantoux test gave negative results. Daily high temperatures, varying from 100 to 104 F., continued for six and one-half months, the only definite complaint being shifting pain in the joints, particularly the knees. Except for an elevated sedimentation rate and for tenderness in the right side of the abdomen, which was noted for the first time five and one-half months after the onset of the polyarticular manifestations, all examinations gave negative results until a large perianal abscess developed. This was incised and drained, and the patient became afebrile. Several weeks after the abscess healed it recurred, but ruptured without surgical intervention.

Three months later the patient was admitted to the hospital with the same type of fever as before. A barium enema suggested an inflammatory infiltration of the terminal ileum, the cecum and the ascending colon. This diagnosis was confirmed at operation, and after resection of the diseased bowel and lymph nodes a side to side ileocolostomy was performed. The patient made a good recovery and has remained well for over a year. The pathologic report was chronic ulcerative and polypoid ileocolitis, Crohn's disease.

The case is reported because of the long period of fever before any localizing manifestation was evident, and it is suggested that regional ileocolitis must be considered in cases of unexplained fever.

LESLIE, Evanston, Ill.

CONGENITAL ATRESIA OF THE ESOPHAGUS WITH TRACHEOESOPHAGEAL FISTULA. CAMERON HAIGHT, Ann. Surg. **120**:623 (Oct.) 1944.

In the anomaly of congenital atresia of the esophagus the upper portion of the esophagus ends as a blind

pouch in almost all instances. The upper end of the lower esophageal segment usually enters the trachea, thus forming a tracheoesophageal fistula. This condition is incompatible with life, as feedings cannot enter the stomach. Furthermore, the feedings and the accumulated secretions in the blind upper segment overflow into the trachea, and death soon results from aspiration pneumonia. The author presents the anatomic and surgical problems involved in the correction of this deformity. A primary anastomosis of the upper and lower esophageal segments was done on 16 of the 24 patients for whom an exploration of the anomaly was undertaken. Six of the 16 patients for whom an anastomosis was performed were living at the time of writing (from seven months to three years and one month after operation), and the reconstructed esophagus is patent in every instance.

In the preoperative treatment the pulmonary status as regards pneumonic complications is carefully determined. From the time that a diagnosis has been made the patient is placed in a prone position with the foot of the bed elevated to favor drainage of oral secretions. A 3 to 5 per cent solution of dextrose in distilled water is given subcutaneously. Ascorbic acid and vitamin K are given routinely. Usually six to twelve hours, and seldom more than twenty-four hours, is sufficient for preoperative treatment.

If the infant was premature by more than two or three weeks or if the weight at birth was less than 4 pounds (1,814 Gm.) operation should probably not be undertaken. An extensive bilateral pneumonic consolidation is a definite contraindication to immediate operation. Other congenital anomalies usually do not contraindicate operation.

BANTIN, Omaha, Neb.

CORRELATION OF THE X-RAY DIAGNOSIS WITH THE OPERATIVE FINDINGS IN SMALL-INTESTINAL OBSTRUCTION. CLAUDE J. HUNT, Radiology **43**:107 (Aug.) 1944.

A collection of gas in the small bowel of the adult may be considered synonymous with obstruction; the typical transverse pattern is not a necessary sign. Gas in small children is of no diagnostic significance. In simple obstruction the distribution of the gas may be centrally located, with a transverse long axis. In loop obstruction this is not true. A stepladder appearance indicates advanced obstruction. In postoperative distention a mechanical factor or ileus may be the causative factor. With the former, only the small bowel is distended; with the latter both the small and the large bowel are distended.

Obstruction due to inflammatory lesions within the abdomen, volvulus, intussusception and external strangulation are briefly discussed. The author states that although the Miller-Abbott tube has fallen into disrepute, he believes it can be used profitably in the treatment of simple adhesive obstruction and for preoperative decompression.

ANSPACH, Chicago.

THE ROENTGEN DIAGNOSIS OF HYPERTROPHIC PYLORIC STENOSIS IN INFANTS. H. W. HEFKE, Radiology **43**:267 (Sept.) 1944.

The author emphasizes as a sign of pyloric stenosis the narrowed prepyloric canal described previously by Meuwissen and Sloof (1932). He considers it the only entirely reliable roentgen finding.

Of 150 infants examined for pyloric stenosis at the Milwaukee Children's Hospital, 68 were operated on after a roentgenographic diagnosis of pyloric stenosis. In all tumors were found.

The author believes that the most important roentgenographic sign is the actual demonstration of the narrowed prepyloric canal by either fluoroscopic examination or roentgenograms. In about 50 per cent of the patients this could not be made out with the fluoroscope. For others who were seen eventually, it was necessary to take several roentgenograms, requiring up to an hour. By this method of repeated examination, the narrowed canal of the pylorus or a part of the duodenal cap could be seen on at least one film, and usually on more than one. The position for the taking of the film was determined with the fluoroscope.

ANSPACH, Chicago.

TWO CASES OF GONOCOCCIC PERITONITIS IN CHILDREN. CARLOS ALBERTO CHAVES DE ARUJO, *Pediat. e Puericult.*, Bahia **13:56** (Sept.) 1943.

Two patients with gonococcic peritonitis were successfully treated by therapy with sulfonamide compounds over a period of five days.

DWYER, Kansas City, Mo.

DIVERTICULA OF MECKEL. EINAR EDBERG, *Svenska läk.-tidning*. **40:2958** (Dec. 17) 1943.

This is a report on 26 patients (16 boys and 10 girls) with Meckel's diverticula. In 5 of them this finding was incidental, at laparotomy for other diseases. Two patients had an open diverticulum at the umbilicus. One of these patients died; the other was discharged healthy. Melena due to ulceration of the mucosa of the diverticulum occurred in 3 patients, who were successfully operated on. In 5 patients there was diverticulitis with signs and symptoms of appendicitis, with a fatal outcome in 1 patient. One patient had Meckel's diverticulum with interocystoma; 5, of whom 2 died, had ileus ex strangulatio; 4 had a diverticulum with intussusception, and 1 had a diverticulum perforated by a fishbone.

WALLGREN, Stockholm, Sweden.

Nervous Diseases

DIFFUSE MENINGEAL SARCOMA. ANTONIO ROTTINO and ROBERT POPPITI, *J. Neuropath. & Exper. Neurol.* **2:190** (April) 1943.

A girl aged 10 years, with one year's history of symptoms and with neurologic evidence of an expanding lesion of the right parietal lobe, suddenly became comatose and died. Gross examination of the brain revealed a thick, plaquelike, nonencapsulated tumor occupying the leptomeninges and the cortex of the dorsolateral surface of the right parietal lobe and adherent to the overlying dura.

Microscopic examination of the tumor revealed that the type and arrangement of the cells were characteristic of meningioma, but in some areas multinucleated giant cells and abundant mitotic figures justified the diagnosis of meningeal sarcoma. Most notable was the fact that numerous columns of cells from the under surface of the neoplasm penetrated the cortex along the course of the blood vessels. The tumor was thickest centrally, where the brain was massively infiltrated. At its periphery the meningeal growth gradually thinned, to become confined to the pia-arachnoid. Elsewhere in the meninges there were focal areas of solid membrane.

The author believes that this case of a malignant meningeal tumor gives support to the opinion expressed by Globus that "in certain conditions, the meninges covering the brain may retain their premature arrangement after birth," and to Weinberger's theory that "the

presence of such sheets of undifferentiated tissue would a priori provide a source for future tumor formation."

CAMPBELL, New York.

[*ARCH. NEUROL. & PSYCHIAT.*]

A COMPARATIVE STUDY OF LOUDNESS, PITCH, RATE, RHYTHM AND QUALITY OF THE SPEECH OF CHILDREN HANDICAPPED BY CEREBRAL PALSY. BERNIECE R. RUTHEFORD, *J. Speech Disorders* **9:263**, 1944.

A group of 48 children with the extrapyramidal type of cerebral palsy and a group of 74 with the pyramidal, or spastic, type were controlled against a group of 69 children without cerebral palsy for the quality, loudness, pitch, rate and rhythm of the voice. Three judges rated the patients on these points. There was little evidence that there is a sharply defined type of speech characteristic of these children. The range of individual differences was wider than that of likenesses. The term characteristic spastic speech should not be used. The children with the two types of cerebral palsy differed in rate and rhythm trends as to the proportion of voices which were loud, low pitched, monotonous or breathy. The group with the extrapyramidal type of cerebral palsy tended toward slower, more jerky speech. The group with the pyramidal type of cerebral palsy contained more loud voices, more low-pitched voices and more monotonous voices. The differences seemed to be related to the control of the breathing apparatus. Differential therapy for patients with cerebral palsy must be based on individual needs.

PALMER, Wichita, Kans.

FAMILIAL CEREBRAL DEGENERATION WITH CORTICAL ATROPHY. H. M. KEITH, *Proc. Staff Meet., Mayo Clin.* **18:499** (Dec. 15) 1943.

Keith performed encephalographic studies on 2 infant siblings. Gross encephalic abnormalities were observed; therefore a diagnosis of diffuse cortical atrophy with progressive mental retardation was made for both infants.

GUTTMAN, New York.

[*ARCH. NEUROL. & PSYCHIAT.*]

CEREBROSPINAL FLUID PROTEIN AND INTRACRANIAL TUMORS. G. PHILLIPS and G. GOSWELL, *M. J. Australia* **1:390** (April 29) 1944.

The incidence of increase in the amount of protein in the cerebrospinal fluid in a series of 161 cases of intracranial tumor was 26 per cent. In search of an explanation of the wide range in percentage of increase reported by other investigators the authors' cases were analyzed with respect to type of tumor cell, to situation and such associated factors as increased intracranial pressure, to vascularity and to direct contact of neoplastic tissue with the circulating ventricular or cerebrospinal fluid.

The only group of tumors in contact with the subarachnoid fluid which produced a constant increase in the level of protein was the cerebellopontile angle tumors growing from the eighth nerve. There appeared to be no direct relation between the cell type, per se, and increase in the level of protein. Neither did there appear to be any direct relation between increased intracranial pressure or duration of increased pressure and overproduction of protein. Vascularity and necrosis of the tumor in the absence of frank hemorrhage did not materially influence the protein content of the subarachnoid fluid.

Although almost any type of intracranial tumor in any situation may raise the level of protein in the cerebrospinal fluid, the authors' experience was that this change seldom took place unless the growth was found either in the region of the sylvian fissure or in the cerebello-pontile angle. Lateral shift either of the ventricles with supratentorial tumors or of the brain stem with angle tumors was constantly associated with an increased level of protein in the subarachnoid fluid.

GONCE, Madison, Wis.

CONTRIBUTION TO THE STUDY OF SPASMUS NUTANS IN INFANCY. LORENZO EXPÓSITO MARTÍNEZ and HUGO GONZÁLEZ DÍAZ, Bol. Soc. cubana de pediat. **15**: 620 (Sept.) 1943.

The authors carefully studied this psychomotor disturbance, which contributes, in their opinion, to more serious nervous disorders developing later in life. The symptom complex is defined and Cruchet's classification outlined in detail. The authors state that spasmus nutans may be a symptom of epilepsy, brain tumor, cerebellar tumor, tuberculous meningitis, tetany, encephalitis, hydrocephalus or acute toxic infections; it also occurs as a reflex during dentition and in intestinal parasitism.

In connection with the etiology of the disease 6 cases are discussed. Expósito Martínez and González Díaz believe in the presence of an anatomic substratum that disappears in most of the cases with the evolution of the nervous system.

KEITH, Rochester, Minn.

Psychology and Psychiatry

SEX DIFFERENCES IN SOCIAL SUCCESS AND PERSONALITY TRAITS. MERL E. BONNEY, Child Development **15**: 63 (March) 1944.

Social success in three groups of fourth grade children was determined by choices made by the pupils. Ratings on personal traits were obtained from pupils and teachers, and self ratings were obtained by the use of the "California Test of Personality, Elementary Form A."

On the whole, sex differences in social success and in personal traits were not found to be large, but there was a high degree of consistency in favor of girls on both kinds of measurements. In only two traits were highly reliable sex differences found. These traits were restlessness and pugnacity, and the boys had the higher scores. These two traits were also the only ones in which the most popular boys had reliably higher averages than the most popular girls. Also on the basis of ratings by teachers, taken separately from ratings by the pupils, the boys were given a 14 per cent higher average than the girls in "fighting." The ratings by teachers gave the girls much higher averages in being tidy, good looking and grownup. On the California Test for Personality the girls had a higher mean score on total adjustment and on all subdivisions of the scale except two, but complete statistical reliability was found on only one part of the test. This was on "social skills," and the advantage was with the girls.

Some relationships between the facts or tendencies observed and the education of boys and girls were pointed out.

EARLY INFANTILE AUTISM. LEO KANNER, J. Pediat. **25**:211 (Sept.) 1944.

This paper reports a study of 20 children (16 boys and 4 girls) who showed features of extreme autistic

aloneness from earliest infancy. All of them came from highly intelligent families. The first thing that the parents of such children notice is the absence of any sort of affective contact. Even within the first few months of life the children fail to show the usual anticipatory reactions to being picked up and the usual adaptation of the body to the person who picks them up. As these children grow older, they become interested in objects which they can handle adequately, but for a long time have no relation whatever to human beings. People are treated as if they were not there, and the children deal with other people's hands or legs as if they were detached objects not related to the people themselves. Some of the children acquire excellent vocabularies, but the words used have no communicative value. When sentences are formed, they are almost exclusively echolalia-like repetitions of things said to them. This results in a peculiar use of pronouns, in that the children speak of themselves as *you* and of other people as *I*. The children are all extremely obsessive, and their excellent rote memory makes them appear at first as child prodigies.

As time goes on most of the children are able to form some degree of compromise with outer reality, learning to carry on a conversation, but they always return to their obsessiveness and aloneness.

The parents are usually people who are much more interested in abstractions than in practical dealings with other human beings; they also show a great deal of obsessiveness.

KANNER, Baltimore.

AN EXPERIMENTAL EVALUATION OF SUGGESTION RELAXATION. RAYMOND CARHART, Speech Monogr. **10**:29, 1943.

Ninety students, 30 men and 60 women, were tested for their palmar resistance on an improved Darrow behavior research box. The subjects were divided into three groups. One group was not instructed to relax; the second group was told to relax without any further instructions, and the third was given detailed instructions on how to relax. There was no sex differentiation in the results. Telling the subjects to lie quietly or simply telling them to relax produced greater relaxation than did the suggestion method. In fact, tensions actually increased under suggestion. During the moment of giving instructions in relaxation, there was increase in tension. Subjects who were requested to speak during the experiment showed immediate increased tension. Subjects who were silent did not show this change.

PALMER, Wichita, Kan.

ACUTE SCHIZOPHRENIA IN CHILDHOOD: REPORT OF A CASE. LOUISE F. W. EICKHOFF, Edinburgh M. J. **51**:201 (April) 1944.

Because of the difficulty of a differential diagnosis, a rare case of acute schizophrenia in childhood, which had formerly been regarded and managed as mental deficiency, is presented. The diagnosis of acute schizophrenia is considered from three viewpoints: the previous history, the clinical picture and the result of the intelligence test. All three sets of data are considered valuable aids in diagnosis. A distinction is made between the moron, who responds to encouragement, and the schizophreniac, who does not, but who does show improvement on immediate retesting. It is important that an early diagnosis be made so that early relief can be given by psychiatric means and a proper emotional adjustment may be made.

NEFF, Kansas City, Mo.

Diseases of the Ductless Glands; Endocrinology

ALLOXAN DIABETES IN THE DOG. M. G. GOLDNER and G. GOMORI, *Endocrinology* **33**:297 (Nov.) 1943.

Experimental diabetes mellitus in dogs has been produced by pancreatectomy and by treatment with anterior pituitary extract. A third, or chemical, type of diabetes may be produced by injection of alloxan (mesoxalyl urea), which has a specific necrosing action on both the pancreatic islet cells and the epithelium of the renal convoluted tubules.

Alloxan diabetes in dogs is characterized by prompt onset of hyperglycemia and glycosuria, within twenty-four to forty-eight hours, sometimes preceded by a short period of hypoglycemia if doses of 75 to 100 mg. per kilogram are given, and later development of hyperlipemia and fatty degeneration of the liver, within ten to twelve days. It differs from anterior pituitary diabetes in that a single injection suffices to produce permanent diabetes and the animals remain sensitive to insulin.

The extremely high levels of blood sugar observed after the administration of doses of 75 to 100 mg. per kilogram suggest that alloxan exerts its diabetogenic action not only through necrosis of the insulin-producing islet cells but by direct effect on the parenchyma of the liver. In totally depancreatized dogs the blood sugar seldom reaches such high values.

Intravenous administration of alloxan to dogs in a single dose exceeding 100 mg. per kilogram caused death of the animals within a few hours. A dose between 75 and 100 mg. per kilogram produced a diabetic-uremic syndrome of which the animals died within one week. A dose of 50 to 75 mg. per kilogram produced typical diabetes without renal lesions. Animals given this amount of alloxan could be kept alive for weeks. The main histologic features of the diabetes produced by alloxan were disappearance of the beta cells from the islets, profound vacuolation of the epithelium of pancreatic ducts and fatty changes in the liver. Doses of 25 mg. per kilogram were without effect.

JACOBSEN, Buffalo.

THE TREATMENT OF HYPERTHYROIDISM IN CHILDREN. C. BERKELEY MCINTOSH, *J. Pediat.* **25**:133 (Aug.) 1944.

Hyperthyroidism in children tends to be a self-limited disease. In spite of this fact, surgical procedure has been the preferred method of treatment for the last twenty years. In recent years, however, some clinicians have been questioning whether thyroidectomy is the best treatment for all children with hyperthyroidism. Dr. W. A. Reilly, of the University of California Medical School, reported in 1940 that about half of his series of 62 patients obtained complete arrest of their disease without surgical intervention.

Of 23 children with hyperthyroidism treated at the University Hospital since 1925, 19 were subjected to subtotal thyroidectomies, and 4 were treated without surgical procedure. The operations resulted in 9 complete arrests, 3 nearly complete arrests, 5 recurrences and 2 deaths. The patients not subjected to operation were all successfully treated by conservative management. The conclusions drawn from this study are that in treating children with hyperthyroidism an adequate trial of medical management should be made before surgical intervention is advised and that for a considerable number of these children operation does not become necessary or desirable.

AUTHOR'S SUMMARY.

Diseases of the Muscles, Bones, Joints and Lymph Glands

A COMPARATIVE STUDY OF MUSCLE ATROPHIES CAUSED BY DENERVATION AND ACUTE INANITION. H. M. HINES, J. D. THOMSON and B. LAZERE, *Am. J. Physiol.* **140**:115 (Oct.) 1943.

A comparative study of the atrophies due to acute inanition and denervation in the tibial nerves and gastrocnemius muscles of albino rats was made by the authors. They found no evidence that prolonged acute inanition resulted in "functional denervation" of skeletal muscle. They observed that the muscles of fasting animals did not exhibit characteristics typical of denervation atrophy, such as the presence of fibrillary activity and the contracture response to injections of acetylcholine. The ratio of the tension elicited by nerve stimulation to that elicited by direct muscle stimulation was the same in fasting as in well nourished animals. The regenerating nerve fibers of fasting animals were able to make functional contacts with muscle units quite as effectively as those of well nourished animals.

STOESSER, Minneapolis.

MYASTHENIA GRAVIS—ITS OCCURRENCE IN A SEVEN YEAR OLD FEMALE CHILD. MELVIN D. YAHR and THOMAS K. DAVIS, *J. Pediat.* **25**:218 (Sept.) 1944.

The authors report the myasthenia gravis syndrome in a young child showing generalized weakness and variable bilateral ptosis. This child was first studied in June 1943, when she was 7 years old, but it would appear that abnormal weakness began much earlier, possibly as early as 14 months. The blood count was within normal limits. The Wassermann and Kline tests of the blood gave negative results. The fasting blood sugar was 93 mg. There were no abnormal findings in the urine. Urinary excretion of creatine was not determined. Roentgenographic examination showed no evidence of thymic enlargement. Chromatic studies of the muscles of the face and of the sternocleidomastoid muscles gave results within normal range. Tests with the faradic current before and after intramuscular administration of neostigmine methylsulfate gave results characteristic of myasthenia gravis. Also the speech test of Viets and Schwab was positive: Without neostigmine the child could count to 25; after injection of neostigmine methylsulfate (0.75 mg.) she counted well above 100.

This patient showed coincidental defective intelligence. On the revised Stanford-Binet form L, the intelligence quotient was 44.

The patient at the time of writing was showing satisfactory therapeutic response to a daily dose of 22 mg. of neostigmine bromide given orally, supplemented by 0.75 mg. of neostigmine methylsulfate given intramuscularly every other day.

YAHR.

OSTEOSARCOMA IN INFANCY. CARLOS DA GAMA, *Pediat. e puericult. Bahia* **13**:49 (Sept.) 1943.

Bilateral and symmetric osteosarcoma of the knees of a child aged 10 years is described. The differential diagnosis in the early stages among bone cysts, white tumor and osteomyelitis is discussed. Osteosarcoma tends to affect long bones at the epiphysis: The lower part of the femur and the upper part of the tibia are frequent sites.

DWYER, Kansas City, Mo.

CASE OF BOECK'S SARCOID. ANNIE SCHONDEL, Nord. med. (Hospitlstid.) **17**:258 (Feb. 13) 1943.

A boy of 2½ years had previously been healthy, but one year before he was seen by the author he had swellings and tenderness in his fingers that persisted. At the examination the second phalanges of the second and third fingers of the right hand and of the third finger of the left hand showed distinct swelling without tenderness. The toes were normal. Slightly enlarged lymph nodes were present in the neck. The internal organs appeared normal under roentgen examination. The tuberculin test gave a negative result. The sedimentation rate of the blood was 5 mm. White cells numbered 12,240, with 51 per cent lymphocytes. Roentgenograms showed disseminated small defects in the affected phalanges, rather typical of Boeck's disease.

WALLGREN, Stockholm, Sweden.

Diseases of the Eye

DIATHERMY COAGULATION IN THE TREATMENT OF ANGIOMATOSIS RETINAE AND OF JUVENILE COATS'S DISEASE: REPORT OF TWO CASES. J. S. GUYTON and F. H. MCGOVERN, Am. J. Ophth. **26**:675 (July) 1943.

The authors report a case of bilateral angiomas of the retinae in which diathermy coagulation gave gratifying results and a case of juvenile Coats's disease in which diathermy treatment apparently checked the progress of the disease.

In the first case, of early angiomas of the retinae of the right eye and advanced angiomas of the retinae of the left eye, the angiomas were obliterated by diathermy coagulation. The sites of the angiomas became scars, and the dilated retinal vessels were reduced in size. Vision was completely preserved in the right eye, and the ophthalmoscopic appearance of the left eye improved, although vision was not regained.

In the second case, of early juvenile Coats's disease of the right eye and complete blindness of the left eye, due to massive exudative retinitis, the left eye was enucleated because of early phthisis. Histologic examination of this eye showed a few areas of capillary proliferation in the retinal lesions, somewhat suggestive of angiomas of the retinae. The primary peripheral lesion, in the retina of the right eye, which had steadily progressed in size for eleven months, was obliterated with diathermy punctures. The site of the peripheral lesion became a scar; edema of the disk and a subretinal exudate below the disk disappeared, and vision was completely preserved.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

NEUROMYELITIS OPTICA. JOSEPH F. SIEGEL, J. Pediat. **25**:328 (Oct.) 1944.

An instance of paraplegia associated with bilateral optic neuritis is reported with the clinical diagnosis of neuromyelitis optica.

A clinicopathologic discussion of neuromyelitis optica is presented, attention being called to its clinical similarity to other demyelinating diseases of the nervous system.

An attempt is made to differentiate neuromyelitis optica clinically from allied disorders.

AUTHOR'S SUMMARY.

Skin Diseases; Allergy

A RAPID TREATMENT FOR SCABIES. ALBERT H. SLEPYAN, J. A. M. A. **124**:1127 (April 15) 1944.

Slepyan treated 189 persons with scabies with benzyl benzoate and followed them for more than fourteen days. No recurrences were noted. Two patients concurrently infected with pediculosis pubis were also cured of their pediculosis by the scabicide.

HENSCHEL, Denver. [ARCH. DERMAT. & SYPH.]

CAUSE AND TREATMENT OF FURUNCULOSIS. PHILIP B. PRICE, J. A. M. A. **124**:1189 (April 22) 1944.

Price believes that a local spread of infection is sufficient to account not only for the features of furunculosis but for its characteristic chronicity. It is his opinion that the usual mode of spread of infection in furunculosis is by discharges, sweat, bathing and friction, which smear the pathogenic organisms over the surface of the skin.

He recommends that an attempt be made to sterilize the skin of the whole contaminated region. Healthy skin can be thoroughly degermed with exactly 70 per cent ethyl alcohol. Price washes the involved area for from twenty to thirty minutes with the alcohol. The optimum time to employ this treatment is in the interval between the healing of one furuncle and the onset of the next. Eleven patients with furunculosis so treated had prompt and permanent relief.

HENSCHEL, Denver.
[ARCH. DERMAT. & SYPH.]

HUMAN DANDER: AN IMPORTANT CAUSE OF INFANTILE ECZEMA. FRANK A. SIMON, J. A. M. A. **125**:350 (June 3) 1944.

Patch tests with human dander elicited positive reactions in 15 of 20 infants and young children with eczema. In 23 noneczematous controls only 1 positive reaction to the patch test was elicited. Prompt clinical improvement appeared in 3 of 4 patients with infantile eczema after institution of measures directed at the avoidance of contact with human dander. In all 4 of them typical eczematous areas were produced on a previously uninvolved area of skin when the mother was instructed to rub her hair on the child's abdomen for two or three minutes twice daily.

HENSCHEL, Denver. [ARCH. DERMAT. & SYPH.]

THE CAUSES OF HAY FEVER OCCURRING BETWEEN THE GRASS AND RAGWEED SEASONS. ROBERT CHOBOT and HAROLD D. DUNDY, J. Allergy **15**:182 (May) 1944.

Chobot stresses the importance of learning what pollens may be present in the air in the preragweed season. If present, even in small quantities, there are a few patients who will be benefited by the addition of a small amount of the extract to the ragweed extract. Sensitivity to the pollen as demonstrated by a skin test is not the only requisite. The patient should be observed during the season to exclude other causative factors.

HOVER, Cincinnati.

A CONSIDERATION OF SOME ALLERGY PROBLEMS. ROBERT A. COOKE, J. Allergy **15**:203 (May) 1944.

This article deals with the problem of allergic dermatitis intelligently and with common sense and candor. The author's conclusions should be helpful in treating the conditions discussed:

Neurodermatitis of older children and adults is only chronic eczema and should be so called.

Contact type eczematous dermatitis is an allergy. Eczema of adults, children and infants, the so-called atopic dermatitis, is also an allergy. The two conditions are immunologically identical.

The method by which contact is established, whether external or internal, is inconsequential. The type of substance, whether protein, oil, resin or complex organic chemical (so long as it is not a primary irritant), is immaterial also.

Patch tests and clinical tests by exposure to the antigen are the only methods available today for etiologic diagnosis.

Since sensitization of the skin is not always general, care must be taken to apply the patch to an area that has been the site of a lesion.

Intradermal or scratch tests must be discarded as diagnostic procedures for eczema, and the terms atopic dermatitis and neurodermatitis should be eliminated from the nomenclature.

HOYER, Cincinnati.

CLINICAL EVALUATION OF ASCORBIC ACID IN THE TREATMENT OF HAY FEVER. SELIAN HEBALD, J. Allergy 15:236 (May) 1944.

Ten patients with hay fever were treated with 250 mg. of ascorbic acid twice a day for a period of four to five weeks during the season of 1943. Definite improvement was shown in only 2 of the cases. No laboratory work was done.

HOYER, Cincinnati.

DEATHS FROM ASTHMA. FRANCIS M. RACKEMANN, J. Allergy 15:249 (July) 1944.

The reports at autopsy on 50 of his own cases of asthma and cases of asthma collected from the literature are reviewed. The patients in 82 of these cases died because of asthma. Most of the deaths occurred after the age of 45, but the typical symptoms and pathologic changes occur in younger persons.

Death from asthma is caused by the development of tough, sticky mucus plugs, which obstruct the bronchi and cause suffocation.

The pathologic picture is characterized by voluminous, distended lungs of bluish gray color, and the cut section shows all bronchi occluded by plugs.

HOYER, Cincinnati.

THE USE OF STRAINED MEATS AS THE PROTEIN BASIS FOR MILK SUBSTITUTES IN THE TREATMENT OF MILK ALLERGY. JEROME CLASER, J. Allergy 15:283 (July) 1944.

Three children with infantile eczema showed improvement with the use of a formula with strained meat as its base. The children had shown no improvement with the use of other milk substitutes. Unfortunately the food that was used is not available commercially. Its composition and the method of its preparation are, however, given in detail.

HOYER, Cincinnati.

ERYTHEMA NODOSUM IN CHILDREN. EDITH M. LINCOLN, JANET ALTERMAN and HYMAN BAKST, J. Pediat. 25:311 (Oct.) 1944.

The total number of cases of erythema nodosum encountered in three large hospital services in the United States is small compared with the numbers reported from northern continental Europe. In the majority of adolescent and adult patients seen in Boston and New York the eruption would seem to be due to infections other than tuberculosis. In the series reported from the children's ward of Bellevue Hospital,

New York, 74 per cent of the children with erythema nodosum reacted positively to the tuberculin test, three to four times the normal incidence, although in only 39 per cent of the cases could tuberculosis be considered definitely responsible for the erythema nodosum. Of 362 patients over 2 years old with active primary tuberculosis, erythema nodosum occurred in 3.6 per cent. The symptom complex of erythema nodosum developed concomitantly with the primary tuberculosis in 2.7 per cent of the cases. It is possible that the apparent contradiction in medical literature concerning the causation of erythema nodosum may be due to the describing of groups of patients of varying ages. The authors of the present article conclude that every child with erythema nodosum should be regarded as potentially tuberculous, but that no child should be finally considered tuberculous without a complete study; that when erythema nodosum occurs in children with active tuberculosis it is commonly associated with the early phases of the disease and that erythema nodosum may be an important aid in the diagnosis of tuberculosis in an individual case. In the United States the condition occurs so uncommonly that its usefulness as a diagnostic aid is much less than in northern Europe.

AUTHORS' SUMMARY.

CONGENITAL, HEREDITARY LYMPHEDEMA (MILROY'S DISEASE). KURT GLASER, J. Pediat. 25:337 (Oct.) 1944.

The author describes 2 cases of Milroy's disease observed at the Milwaukee Children's Hospital and gives a brief review of the entire subject, including the high lights of the literature.

A disease most likely Milroy's disease was first described by J. Hille, in Germany about the middle of the last century, and was again described by Milroy in 1890 in the United States. Osler gave it the name Milroy's disease. In 1928, after thirty-five years of observation, Milroy himself published a report about the same family he had described in 1892 and discussed the condition in general.

The condition is defined as congenital, hereditary edema without tenderness or painfulness and without constitutional symptoms. It is of rare occurrence and usually affects several members of the same family. The cause is unknown, and several theories have been suggested. The symptom is pitting edema of one or both legs, never extending above Poupart's ligament. There are no significant laboratory findings. The pathologic-microscopic manifestations are enlarged lymph spaces with increase in the surrounding fibrotic tissue. The course is chronic and progressive. The treatment is palliative. It consists of applying pressure bandages to prevent further swelling.

A white boy aged 4 years at the time of this report and his sister, one year younger, are described. Both children had had swelling of the feet since birth. The extent of the swelling varied, being influenced to a slight degree by the amount of exercise and by the application of pressure. The boy showed a marked swelling of the prepuce, which was remedied by circumcision.

Complete laboratory study of the urine, the chemistry of the blood (chlorides, nonprotein nitrogen, cholesterol, calcium, phosphorus, phosphatase, total protein and albumin and globulin) and the serology of the blood, as well as the wheal absorption test, gave normal results.

Roentgenographic studies showed normal formation of bones in both children. Microscopic examination of the boy's foreskin revealed large structures resembling

bling lymphatics and dense collagen fibers, a picture typical of the condition as described by other authors.

The treatment consisted of application of bandages of different types, all with the purpose of reducing the amount of edema by pressure. The result was, as was expected, only slight and of temporary value.

The paper reports 2 typical cases of Milroy's disease, demonstrating the absence of a causative constitutional disorder. It describes the histologic changes in this condition, throwing some light on the theories of causation. Two photographs show the edema of the legs.

GLASER, Milwaukee.

PSEUDOPSEUDOMATOUS NODOSUM DUE TO SULFATHIAZOLE THERAPY. RAUL CIBILS AGUIRRE, JULIO R. CALCARONI and JULIO A. TAHIER, Arch. argent. de pediat. 20:468 (Dec.) 1943.

In 4 children treated with sulfathiazole an eruption resembling erythema nodosum developed. The dose of sulfathiazole administered varied from 0.1 to 0.2 Gm. per kilogram of body weight. The eruption was easily distinguished from erythema nodosum because the nodules were smaller and more pallid. Lack of spontaneous pain was characteristic, as was lack of pain on palpation. The eruption had a tendency to spread not only on the extremities but over the entire surface of the body. The differential diagnosis was established on the basis of the fact that the lesions appeared between the second and tenth days of treatment with sulfathiazole and the transient evolution of the condition. The rash reappeared when the treatment was started again (in 2 cases out of 3). Obviously the lack of history of tuberculosis and the negative reactions to tuberculin were helpful. The impression of the authors is that the prognosis of this condition is favorable. Patients were treated with forcing of fluids and withdrawal of the drug.

CASSORLA, San Francisco.

ALLERGY OF THE CHILD. JOSÉ J. PEDRERA, Bol. Soc. cubana de pediat. 15:600 (Sept.) 1943.

The article presents a rather complete review of the problem, of allergy in children, starting with the definition and discussing the relation to anaphylaxis, the nature of the allergic phenomenon, the different offenders, such as drugs, food, bacteria and so forth, and also the variations according to localization of shock tissue in different organs—respiratory (asthma), skin (eczema) and so forth. Also mentioned is the eczema-prurigo-asthma syndrome described by Rash, as well as the anaphylactic shock of acute onset following ingestion of food, with vomiting, severe abdominal cramps, diarrhea, circulatory collapse and even death as described by Finkelstein. Other symptom complexes are discussed, e. g., gastric disorder, mucus colitis, angioneurotic edema, toxemic allergy with predominantly nervous symptoms, etc. The importance in etiologic diagnosis of a detailed history is pointed out.

KEITH, Rochester, Minn.

Miscellaneous

THE STERNOMASTOID SIGN. A. W. BRANWOOD, Edinburgh M. J. 51:152 (March) 1944.

The author cites R. R. Trail as the first to describe the sternomastoid sign in a discussion of the early diagnosis of tuberculosis in *Lancet* for 1942.

To bring out this sign, the patient's head is supported, and he is told to look straight to the front. A positive sign consists of tenseness of the tendinous portion of the sternomastoid muscle on one side greater than that of its fellow. The significance of the sign is that it denotes displacement of the mediastinum to the side on which the tenseness is found. Branwood cites cases, in 2 of which the patients were children. He feels that this sign may be helpful.

NEFF, Kansas City, Mo.

Book Reviews

Mitchell's Pediatrics and Pediatric Nursing. Revised by Robert A. Lyon, M.D., and Winifred Kaltenbach, B.A., R.N. Price, \$3.00. Pp. 504, with 97 figures and 32 tables. Philadelphia: W. B. Saunders Company, 1944.

The opening chapter of this book depicts the evolution which preceded the refinements of technic in present day methods of care of children. The student learns that children require protection and guidance in order to develop into well and useful citizens. In achieving that goal the nurse has a privileged role to fill.

Physical growth and development, mental, nervous and emotional development and mental hygiene are presented in chapters 2, 3 and 4. The adult's attitude is rightly emphasized, since it is of major importance in the life of a child.

In chapters 5, 6 and 7 the subject of nutrition is covered adequately. The subject of abnormalities of nutrition, which in the 1939 edition was placed under nutrition, now appears under diseases and abnormalities, which is an improvement.

The chapter on children in the home acquaints the student with the child's life in his usual surroundings and describes the adjustments necessary in the home when the child is ill.

Eighty pages are devoted to children in the hospital. Desirable approaches to and management of the child, therapeutic procedures and diagnostic procedures are well presented. Setting up the details of technical procedures is the task of the instructor of pediatric nursing in each school. Throughout these pages there are valuable hints and suggestions for caring for the sick child. In a few instances sketches would be a better medium than photographs to depict equipment.

The subject of abnormalities and diseases is presented in an orderly manner, proceeding from pathologic conditions in premature and other newborn infants through abnormalities in nutrition to the diseases involving the various systems of the body. Throughout the 247 pages devoted to this subject there are numerous pictures and tables. The photographs of rashes, however, have lost their value through not being in color. The tables and diagrams are excellent and will aid the student materially.

A description of the child in the community is pertinent. The functions of a health department are explained, and graphs and tables show the causes of death in various age groups. Institutions and agencies that substitute for parents in caring for the child are discussed thoroughly.

There is an appendix replete with needed information, well tabulated and arranged for ready reference.

This book is readable and practical, and throughout its pages the reader feels a fine regard for the child. No one will close the book without realizing the necessity for the care of children and the dire need of adequate instruction in health, especially for prospective parents.

The text is good and is supplied with ample bibliographies. The subjects treated by the curriculum guide for schools of nursing in the five units of instruction under the nursing care of children are adequately covered in the arrangement in six units by the present authors. Sections of the text will be of help to parents. Public health nurses and private duty nurses could well use it for reference. A review of this book by medical students will enable them to adapt themselves more readily to children in the hospital.

Small Community Hospitals. By Henry J. Southmayd and Geddes Smith. Price \$2.00. Pp. 182, with no illustrations. New York: The Commonwealth Fund, 1944.

If there are any authorities on rural or community hospitals the Commonwealth Fund should qualify as one of them, for it has assisted in the building of 14 such hospitals in the United States. It is with this experience and with the problem faced by smaller communities that this book deals. Although there has been a rapid growth in the number of small hospitals, this growth will without doubt increase in the future.

The actual physical plant of the hospital presents only a small part of the problem that a community must consider. First, the needs of the community must be studied; second, an adequate and cooperative medical staff must be organized, and, third, a sound financial basis must be established. Only when these preliminary steps have been taken can the physical plant of the hospital and its administration be considered.

The authors deal intelligently with all these problems as they have met them in the field. From this experience they point out how the minimum standards set up by the American College of Surgeons can be met. There are chapters on the rural hospital as a community institution, the rural hospital and the medical team, organization and administration, hospital finances, the hospital plant and the hospital and the countryside.

Although this book is primarily for the nonprofessional person, medical students and physicians in practice should read it to obtain a better understanding of the problems and responsibilities of hospitals large and small. "The modern community hospital under voluntary auspices is a middle of the road merger of the charity institution and a private facility. It sells services when it can to patients who are willing and able to pay, and gives service—at community expense—to those who cannot pay."

All About Feeding Children. By Milton J. E. Senn, M.D., and Phyllis Krafft Newill. Price, \$2.50. Pp. 269, with 1 table. New York: Doubleday, Doran and Company, 1944.

At long last here is a book for mothers, written in a pleasing style, that covers meticulously all the everyday problems of nutrition from birth to adolescence. The authors offer their book as a supplement to the

advice of the attending physician, thereby relieving him from the duty of giving time-consuming individual verbal instructions on preparations of food, the technic of feeding and the psychologic approach to new foods.

The title, "All About Feeding Children," is well justified. The authors discuss in detail every phase of what, when and how to feed infants and the other members of the younger generation.

The chapter on the breast-fed baby is commendable. It states that the pendulum is swinging back so that mothers now take pride in nursing their babies as nature intended they should. This chapter is full of good common sense and strongly urges every mother to nurse her baby if possible. This advice for nursing mothers, plus the technic for establishing and maintaining milk supply, should be available to every mother before she leaves the hospital.

The suggestions and directions on the bottle-fed infant and the chapter on preparing special formulas are most complete. The latter half of the book, oddly enough, might be described as the first real cookbook exclusively for children.

The authors approach the psychologic aspects of feeding children in the sympathetic modern way. They are distinctly liberal and broad minded and avoid controversial subjects.

No medical advice is given, and they warn against prescribing at home and against accepting advice from any one except the physician in charge. They condemn the hit and miss giving of vitamins and minerals.

In the chapter on the so-called dysfunctions associated with eating the authors consider all the minor illnesses, ailments and idiosyncrasies in connection with faulty diets, incorrect handling and preparing of foods and wrong eating habits. Here they again emphasize the necessity for direct supervision by a physician in all but the mildest conditions. They discuss colic, constipation, diarrhea, vomiting, hiccups, allergy, anorexia and thumb sucking. Many of the common points which the authors bring out are not so well known by all members of the medical profession, but that they could derive benefit from reading this chapter.

This book, being a work of reference, has an excellent index and a glossary of the terms usually left unexplained to mothers.

The book may be recommended unreservedly to all mothers and to physicians.

Stuttering: Significant Theories and Therapies.

By Dr. Eugene F. Hahn. Price, \$2. Pp. 177, no illustrations. Stanford University: Stanford University Press, 1943.

This volume is a summary of the views of eighteen American and seven European authorities on stuttering.

Its purpose is to facilitate study of the literature. Although several outstanding authorities, such as Orton and Janet, have been omitted, the author has presented the views of all of the schools of thought on the subject.

In reading this volume one is impressed with the widely divergent, authoritative, positive views on the cause, nature and treatment of stuttering. In the appendix the author describes briefly the procedure followed in his clinic in Detroit.

The book is well written, instructive and interesting. A bibliography is appended.

News and Comment

GENERAL NEWS

Physicians Certified by American Board of Pediatrics.—The following physicians were certified as specialists by the American Board of Pediatrics after the examinations in St. Louis and New York on Nov. 8 and 9:

Dr. Chester J. Antos, Jefferson City, Mo.; Dr. Stuart Lane Arey, Minneapolis; Dr. Hans C. S. Aron, Chicago; Dr. Katharine Howard Baird, Wauwatosa, Wis.; Dr. Felix P. Basch, Chicago; Dr. John H. Benward, Portland, Ore.; Dr. Mary Scarborough Boyden, Lawrence, Kan.; Dr. Rowine Hayes Brown, Chicago; Dr. John F. Burn, Butler, Pa.; Dr. Mollie Cholfin, Sacramento, Calif. (formerly Cleveland); Capt. Richard D. Cutter, Santa Ana, Calif. (formerly San Francisco); Dr. Parker Dooley, Chicago; Dr. Genevieve Delfs Ewing, Youngstown, Ohio; Lt. Herbert William Fink, San Diego, Calif. (formerly Detroit); Dr. Joseph Edward Ghory, Cincinnati; Dr. Evelyn Smith Harris, Minneapolis; Dr. Allan Janney Hill, Jr., New Orleans; Dr. Oliver W. Hosterman, Columbus, Ohio; Dr. Gerda B. Irving, Chicago; Capt. Philip J. Kozinn, Excelsior Springs, Mo. (formerly New York); Lt. Maurice W. Laufer, Galesburg, Ill. (formerly Yellow Springs, Ohio); Dr. Frederick H. Maurer, Peoria, Ill.; Dr. Martin G. Neely, Fairfield, Ala.; Dr. Richard Robert O'Toole, Pittsburgh; Dr. Glenn B. Patrick, Elkhart, Ind.; Capt. Joseph H. Patterson, Fort McPherson, Ga. (formerly Nashville, Tenn.); Lt. Edward B. Plattner, Fort McPherson, Ga. (formerly Chicago); Dr. Weldon A. Price, Arlington, Va.; Dr. Maryelda Rockwell, Clinton, Iowa; Dr. Iwan Rosenstern, Evanston, Ill.; Dr. George Wilbur Salmon, Houston, Texas (formerly St. Louis); Dr. Alice Schiff (name formerly Schiff-Goldstein), Los Angeles; Dr. Helmut P. G. Seckel, Chicago; Dr. Clark Workman Seely, Kansas City, Mo.; Dr. Francis Scott Smyth, San Francisco; Dr. Homer Fauquier Wier, Rockford, Ill.; Dr. Dorothy B. Wyvell, Dallas, Texas.

Directory of Pediatric Societies *

INTERNATIONAL

INTERNATIONAL ASSOCIATION OF PREVENTIVE PEDIATRICS

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

INTERNATIONAL CONGRESS OF PEDIATRICS

President: Dr. Henry F. Helmholtz, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Charles F. McKhann, University Hospital, Ann Arbor, Mich.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: Boston. Time: Postponed indefinitely.

INTERNATIONAL CONGRESS FOR THE PROTECTION OF INFANCY

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

ARGENTINE PEDIATRIC SOCIETY OF BUENOS AIRES

President: Dr. Martin Ramón Arana, 1809 Rodríguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Largaia, Cerrito 1179, Buenos Aires.

ASSOCIAÇÃO PAULISTA DE MEDICINA, SECTION ON PEDIATRICS

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Paulo de Barros Franca, Av. Brigadeiro Luiz Antonio 393, 1º Andar, São Paulo, Brazil.

BRITISH PAEDIATRIC ASSOCIATION

President: Prof. L. G. Parsons, 58 Calthorpe Rd., Five Ways, Birmingham.
Secretary: Dr. Donald Paterson, 27 Devonshire Pl., London, W. 1.

DANISH PEDIATRIC SOCIETY

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

NEDERLANDISCHE VEREENIGING VOOR KINDER- GENEESKUNDE

President: Dr. J. H. G. Carstens, Servaasbolwerk 14^a, Utrecht.
Secretary: Dr. R. P. van de Kastele, Laan van Poot 340, 's Gravenhage.
Place: Different places. Time: Three times a year.

PAEDIATRICKÝ SPOLOK NA SLOVENSKU

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. S. Rosentaum, 26 Bialkstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Angel A. Aballí Arellano, 17 No. 609 Vedado, Habana.
Secretary: Dr. Julio G. Cabrera Calderin, Hospital Mercedes L y 21 (Vedado), Box 2430, Habana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Fernando López Clares, 12/a. Medellín 191, Mexico.
Secretary: Dr. Jesus Gómez Pagola, Versalles 64, Mexico.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. E. Santos Mendoza.
Secretary: Dr. P. Oropezz, Hospital de Niños, Caracas.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres
Time: 4:30 p. m., third Thursday of every month.

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Jose Alberto Praderi, Eduardo Acevedo 1132, Montevideo.
Secretary: Dr. Alfredo Ramon Guerra, Paysandú 824, Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.
Place: Philadelphia. Time: June 18-22, 1945.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Joseph S. Wall, 1864 Wyoming Ave. N. W., Washington, D. C.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.

AMERICAN HOSPITAL ASSOCIATION, CHILDREN'S
HOSPITAL SECTION

Chairman: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly, Mass.

AMERICAN PEDIATRIC SOCIETY

President: Dr. James L. Gamble, 300 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES
OF CHILDREN

President: Dr. R. R. Struthers, 906 Drummond Medical Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Edward M. Bridge, 219 Bryant St., Buffalo, N. Y.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia 46.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Eugene Smith, 385-24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Warren R. Sisson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. C. G. Ashley, 833 S. W. 11th Ave., Portland, Ore.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. Arild E. Hansen, University of Minnesota, Minneapolis.
Secretary-Treasurer: Dr. Albert V. Stoesser, 205 W. University Hospital, Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester.
Time: January, April, July and October.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver.

SOUTHERN MEDICAL ASSOCIATION, SECTION
OF PEDIATRICS

Chairman: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.
Secretary: Dr. Angus McBryde, 604 W. Chapel Hill St., Durham, N. C.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Amas Gipson, 948 Forrest Ave., Gadsden.
Secretary-Treasurer: Dr. Ruth Berrey, 2021-6th Ave. N., Birmingham.

ARIZONA PEDIATRIC SOCIETY

President: Dr. Vivian Tappan, San Clemente, Tucson.
Secretary: Dr. Hilda Kroeger, Arizona State Health Dept. (Maternal and Child Welfare Division), Phoenix.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION
ON PEDIATRICS

Chairman: Dr. William C. Deamer, University of California Hospital, San Francisco.
Secretary: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Ludo Von Meysenbug, Box 3356, Daytona Beach.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. T. F. Davenport, 104 Ponce de Leon Ave. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB
OF CONNECTICUT

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Time: Three meetings a year.

ILLINOIS STATE MEDICAL SOCIETY, SECTION
ON PEDIATRICS

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Mark L. Floyd, Children's Hospital, Iowa City.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

**MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION
ON PEDIATRICS**

Chairman: Dr. A. Clement Silverman, 608 E. Genesee St., Syracuse.
Secretary: Dr. Albert G. Davis, 307 Gas and Electric Bldg., Utica.

**MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA,
PEDIATRIC SECTION**

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

**MICHIGAN STATE MEDICAL SOCIETY,
PEDIATRIC SECTION**

Chairman: Dr. Charles F. McKhann, University Hospital, Ann Arbor.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. John L. Gedgoud, University of Nebraska Hospital, Omaha.
Secretary-Treasurer: Dr. Gerald C. O'Neil, 640 City National Bank Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Arthur H. London, 1105 W. Main St., Durham.
Secretary: Dr. Jay M. Arena, 604 W. Chapel Hill St., Durham.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Ben H. Nicholson, 301 N. W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Lonita Boggs, 301 E. Coffee St., Greenville.
Secretary-Treasurer: Dr. Hilla Sheriff, Wade Hampton Office Bldg., Columbia.

TEXAS PEDIATRIC SOCIETY

President: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. L. E. Sutton Jr., Medical College Hospital, Richmond.
Secretary: Dr. Emily Gardner, 1100 W. Franklin St., Richmond.

**WEST VIRGINIA STATE MEDICAL SOCIETY,
SECTION ON PEDIATRICS**

President: Dr. Andrew Amick, 1021 Quarrier St., Charleston.
Secretary: Dr. A. A. Shawkey, Professional Bldg., Charleston.

LOCAL

**ACADEMY OF MEDICINE OF CLEVELAND
PEDIATRIC SECTION**

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. I. B. Silber, 10465 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

**ACADEMY OF MEDICINE, TORONTO,
SECTION OF PEDIATRICS**

President: Dr. I. Nelles Silverthorne, 170 St. George St., Toronto, Canada.
Secretary: Dr. G. P. Hamblin, 2333 Bloor St. W., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry J. Cohen, 1975 Walton Ave., New York.
Secretary: Dr. Walter Levy, 12 E. 88th St., New York.
Place: Concourse Plaza Hotel, 161st St., and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Harry A. Naumer, 37-8th Ave., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Granada Hotel. Time: Fourth Wednesday of October, November, February, March and April.

BUFFALO PEDIATRIC SOCIETY

President: Dr. A. Wilmot Jacobsen, 187 Bryant St., Buffalo N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Edward J. Wynkoop, 501 James St., Syracuse.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Morley D. McNeal, 2 N. Sheridan Rd., Highland Park, Ill.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

CINCINNATI PEDIATRIC SOCIETY

Secretary: Dr. T. Selkirk, 3530 Reading Rd., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati.
Time: On call.

President: Dr. Lloyd K. Felter, 3144 Jefferson Ave., Cincinnati.

DALLAS PEDIATRIC SOCIETY.

President: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas, Texas.

Secretary-Treasurer: Dr. Gladys J. Fashena, 4585 Bel-
fort, Dallas, Texas.

Place: Bradford Baby Hospital. Time: 1 p. m., second
and fourth Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. John J. Pollack, 650 Maccabees Bldg.,
Detroit, Mich.

Secretary: Dr. Philip J. Howard, 2799 W. Grand Blvd.,
Detroit, Mich.

Place: Wayne County Medical Society. Time: 8:30
p. m., first Wednesday of each month from October
to June, inclusive.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRICS
SECTION (ATLANTA, GA.)

Chairman: Dr. Don F. Cathcart, 478 Peachtree St.
N. E., Atlanta.

Secretary: Dr. Harry Lange, 478 Peachtree St., N. E.,
Atlanta.

Place: Academy of Medicine, 38 Prescott St. N. E.
Time: Second Thursday of each month from October
to April, 8 p. m.

HOUSTON PEDIATRIC SOCIETY

President: Dr. Raymond Cohen, 2300 Caroline St.,
Houston, Texas.

Secretary: Dr. Betty Moody, 526 Richmond Rd.,
Houston, Texas.

Place: College Inn, Houston. Time: Fourth Monday
of each month.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Edwin H. Schorer, 1103 Grand Ave.,
Kansas City.

Secretary: Dr. H. E. Petersen, Kirkpatrick Bldg., St.
Joseph, Mo.

Place: Kansas City General Hospital. Time: On call.

LOS ANGELES COUNTY MEDICAL ASSOCIATION,
PEDIATRIC SECTION

President: Dr. Oscar Reiss, 2200 W. 3d St., Los
Angeles.

Secretary-Treasurer: Dr. Elena Boder, 1830½ Lucille
Ave., Los Angeles.

Place: Los Angeles County Medical Headquarters, 1925
Wilshire Blvd. Time: Second Monday of February,
April, June, October and December.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND
THE ACADEMY OF MEDICINE OF BROOKLYN,
PEDIATRIC SECTION

President: Dr. Abraham M. Litvak, 1145 Eastern Park-
way, Brooklyn.

Secretary: Dr. Harold Levy, 750 St. Marks Ave.,
Brooklyn.

Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m.,
fourth Monday of each month, October to April,
inclusive.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC.,
SECTION ON PEDIATRICS

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens
Village, N. Y.

Secretary-Treasurer: Dr. Edith A. Mittell, 144-33th
Ave., Flushing, N. Y.

Place: Queens County Medical Bldg., Forest Hills,
N. Y. Time: Third Monday of October, January,
March and May.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA,
SECTION ON PEDIATRICS

President: Dr. Harry A. Spigel, 2647 Connecticut Ave.,
Washington, D. C.

Secretary-Treasurer: Dr. Perry W. Gard, 2520 Wood-
ley Rd., Washington, D. C.

Place: Medical Society Bldg., 1718 M St. N. W. Time:
8 p. m., fourth Thursday of every month.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. F. T. Mitchell, 376 S. Bellevue Ave.,
Memphis, Tenn.

Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madi-
son Ave., Memphis, Tenn.

Place: John Gaston Hospital. Time: Quarterly.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. M. G. Peterman, 411 E. Mason St.,
Milwaukee 2.

Secretary-Treasurer: Dr. B. J. Malnekoff, 3213 N.
Marietta Ave., Milwaukee.

Place: Milwaukee Athletic Club. Time: Second Wednes-
day of each alternate month, beginning with February.

NEW YORK ACADEMY OF MEDICINE, SECTION
OF PEDIATRICS

Chairman: Dr. Howard Craig, 175 E. 79th St., New
York.

Secretary: Dr. Alfred E. Fischer, 73 E. 90th St., New
York.

Place: New York Academy of Medicine, 2 E. 103d St.
Time: Second Thursday of each month from October
to May, inclusive. 8:30 p. m.

NORTHERN CALIFORNIA AFFILIATES

President: Dr. Crawford Bost, 400 Post St., San
Francisco.

Secretary: Dr. William A. Reilly, 384 Post St., San
Francisco.

Time: Second Thursday of September, November,
January, March and May.

OKLAHOMA CITY PEDIATRIC SOCIETY

President: Dr. William M. Taylor, 1200 N. Walker
St., Oklahoma City.

Secretary: Dr. G. R. Felts, 625 N. W. 10th St., Okla-
homa City.

Place: Oklahoma Club. Time: Third Thursday of
each month.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Carl Fischer, Greene and Coulter Sts.,
Germantown, Philadelphia.

Secretary: Dr. Sherman Little, 1740 Bainbridge St.,
Philadelphia.

Place: College of Physicians, 19 S. 22d St. Time:
Second Tuesday in January, March, May and
November.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown, Pa.

Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh.

Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Stanley Meade, 913 Floyd Ave., Richmond, Va.

Secretary-Treasurer: Dr. Louise Galvin, 214 S. Boulevard, Richmond, Va.

Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Herbert Soule, 122 Rutgers St., Rochester, N. Y.

Secretary-Treasurer: Dr. Jerome Glaser, 300 S. Goodman St., Rochester, N. Y.

Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Jerome Diamond, 508 N. Grand Ave., St. Louis.

Secretary-Treasurer: Dr. Mary A. McLoon, 403 Humboldt Bldg., St. Louis.

Place: St. Louis Medical Society Bldg. Time: First Friday of each month from November to June.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Frederick B. Joy, Stimson Bldg., Seattle.
Secretary: Dr. Sherod M. Billington, Medical Dental Bldg., Seattle.

Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.

Secretary: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.

Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Campbell Harvey, 35 W. Huron St., Pontiac, Mich.

Secretary: Dr. Harry A. Towsley, University of Michigan, Department of Pediatrics and Communicable Diseases, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRICS SECTION (NEW YORK)

President: Dr. John B. Ahcuse, 27 Ludlow St., Yonkers, N. Y.

Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.

Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.

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